



Advancing Innovation and Convergence In Cancer Research

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Office of the Director, National Cancer Institute (NCI)
National Institutes of Health (NIH)



2014 ASEE Engineering Research Council Annual Meeting

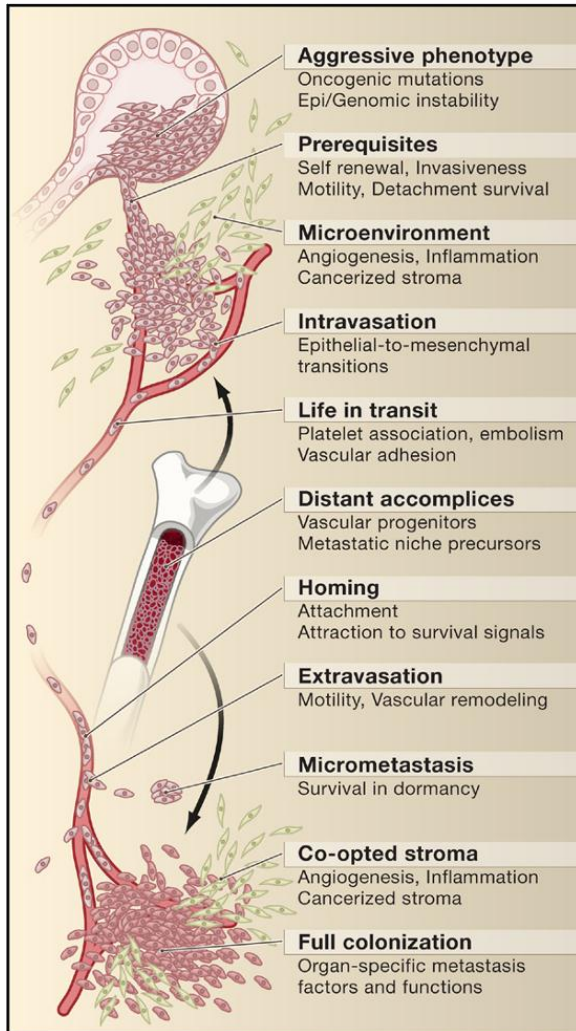
Change and Research Opportunities: Perspectives from NIST, DOE, NGA, and NCI

March 18, 2014



What is It?

Tumor, Cancer, and Metastasis

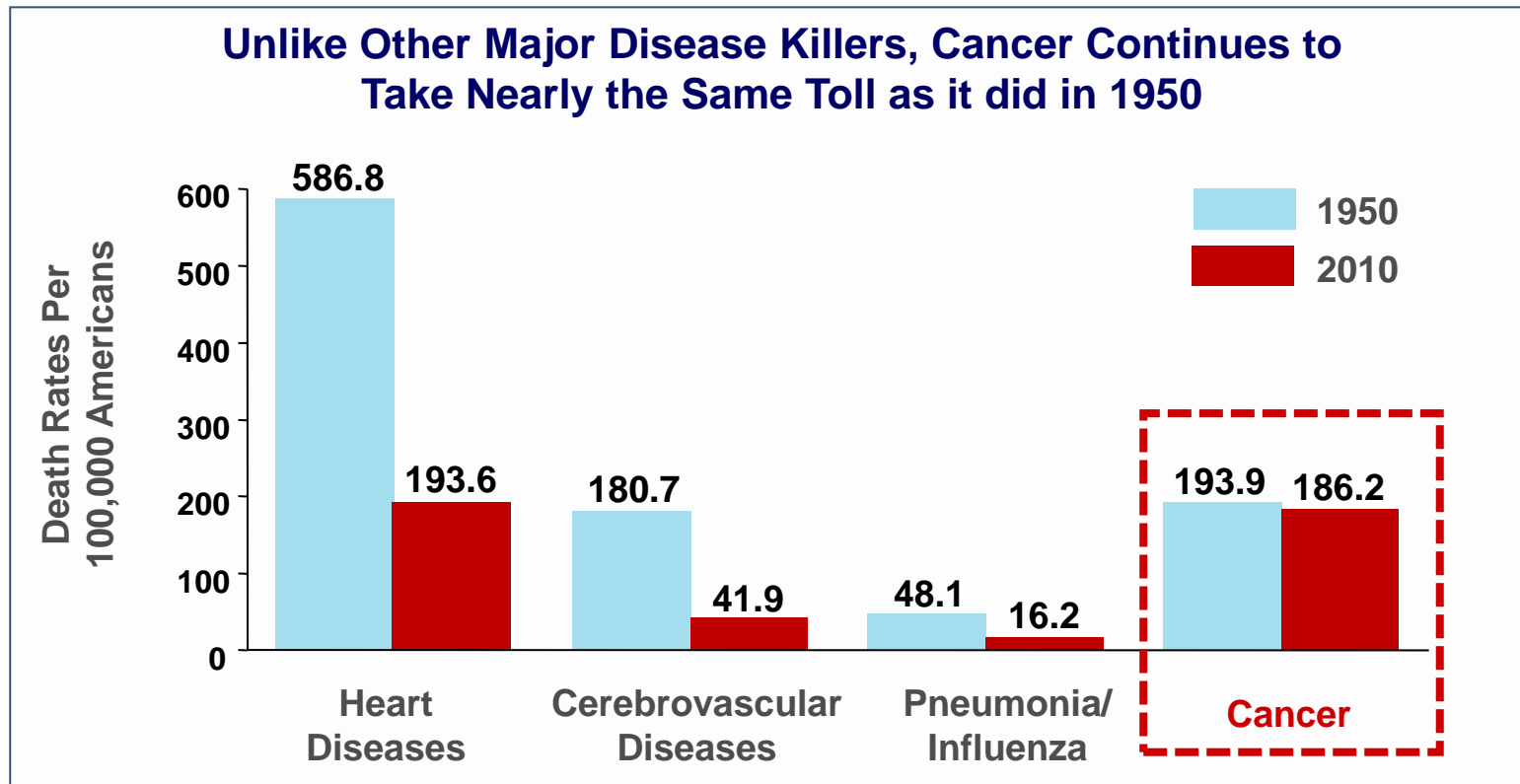


Organ Site	All Stages	Localized	Regional	Distant
Prostate	99	100	100	28
Breast	89	99	84	24
Ovary	44	92	72	27
Uterine Cervix	68	91	57	16
Melanoma	91	98	62	16
Urinary Bladder	78	70	33	5
Kidney	72	92	64	12
Colon and rectum	65	90	70	13
Esophagus	17	39	21	4
Lung and bronchus	17	54	26	4
Liver	16	29	10	3
Pancreas	6	24	9	2

“...>90% of deaths is caused by disseminated disease or metastasis...”

In the U.S., Cancer Continues to Represent an Enormous Burden

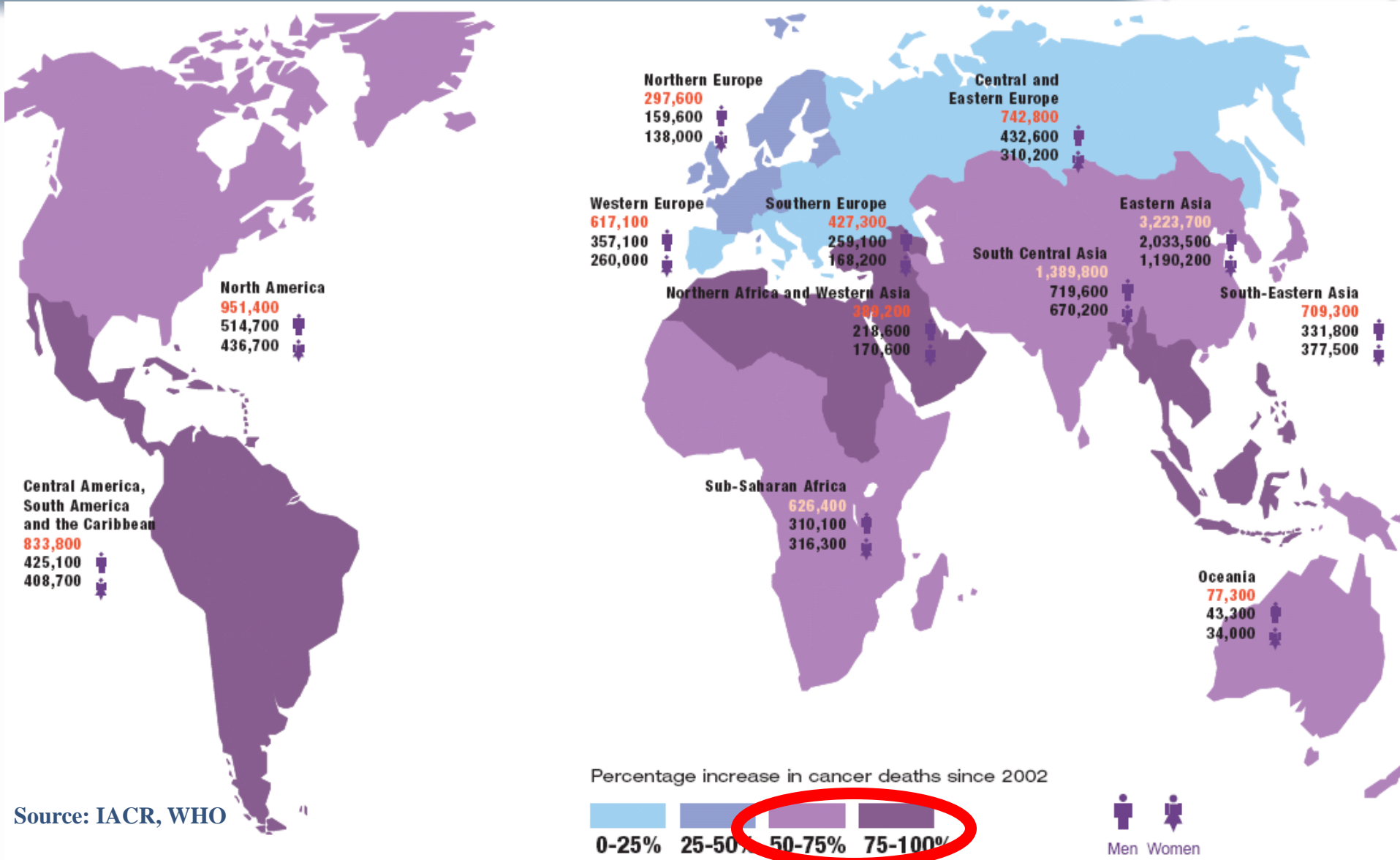
- **574,743** Americans died of cancer in 2010 (**585,720** projected for 2013)
- **1,665,540** Americans will be newly diagnosed with cancer in 2014 (projected)
- **\$216.6 billion** in 2009 for cancer healthcare costs (**\$86.6 billion** for direct medical)



Source for 2014 projected deaths and diagnoses: Siegel et. al, Cancer Statistics, 2014

Source for 2010 age-adjusted death rate: National Center for Health Statistics, National Vital Statistics Report, Dec 2013

Global Burden: By 2020, Cancer Incidence 16 M/yr (Mortality 10 M/yr)



Unprecedented Amount of Scientific Knowledge: Omics(ssss)

A map of human genome variation from population-scale sequencing

The 1000 Genomes Project Consortium*



2001



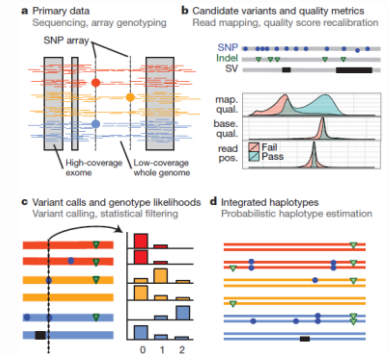
2010

NATURE

1 NOVEMBER 2012

An integrated map of genetic variation from 1,092 human genomes

The 1000 Genomes Project Consortium*



2012

1923

2005

49,024 pubs

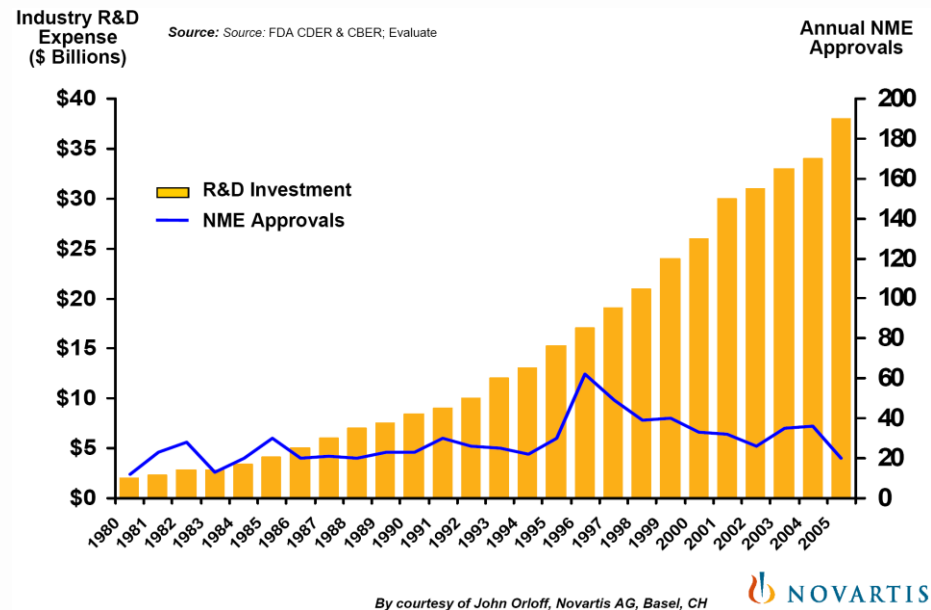
54,587 pubs

87,793 pubs

38,506 pubs

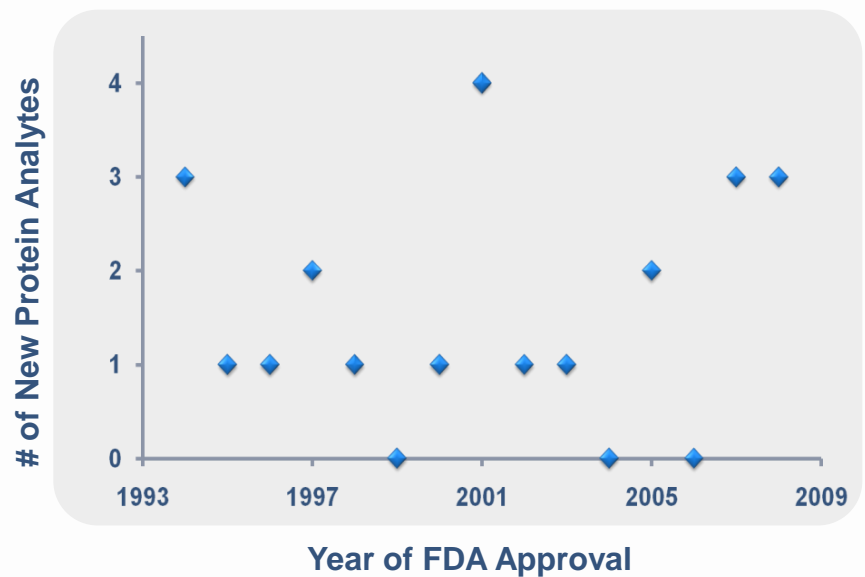
Is More Knowledge Yielding More Solutions for Patients?

Drug Discovery and Development



- 10 – 15 years at ~ \$1.8 billion*
- 2007: 19 NMEs [lowest since 1983]
- 2008: 21 NMEs [29% new-in-class]
- 2009: 24 NMEs [17% new-in-class]

Diagnostic Biomarkers



- Averaging 1.5 FDA approvals per year†
- 1000's of samples
- Balancing complexity of biology against heterogeneity of patients

Maybe...but can it be more efficient?

National Institutes of Health (NIH): 27 Institutes and Centers



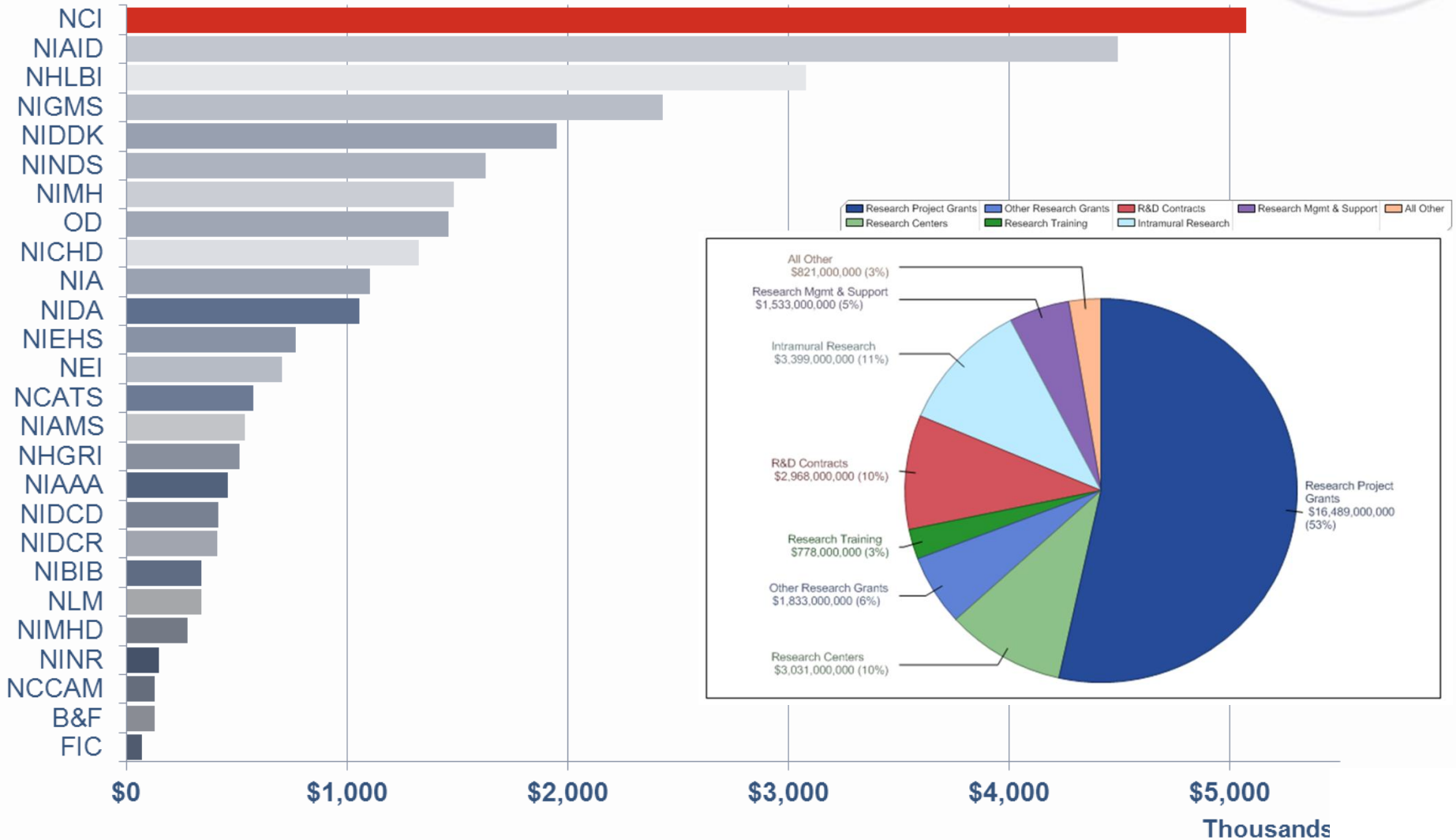
NIH Budget ~ \$30.8 Billion (FY12)

- ~82% for extramural support
- ~63,000 grants and contracts

NCI Budget ~ \$ 5.07 Billion (FY12)

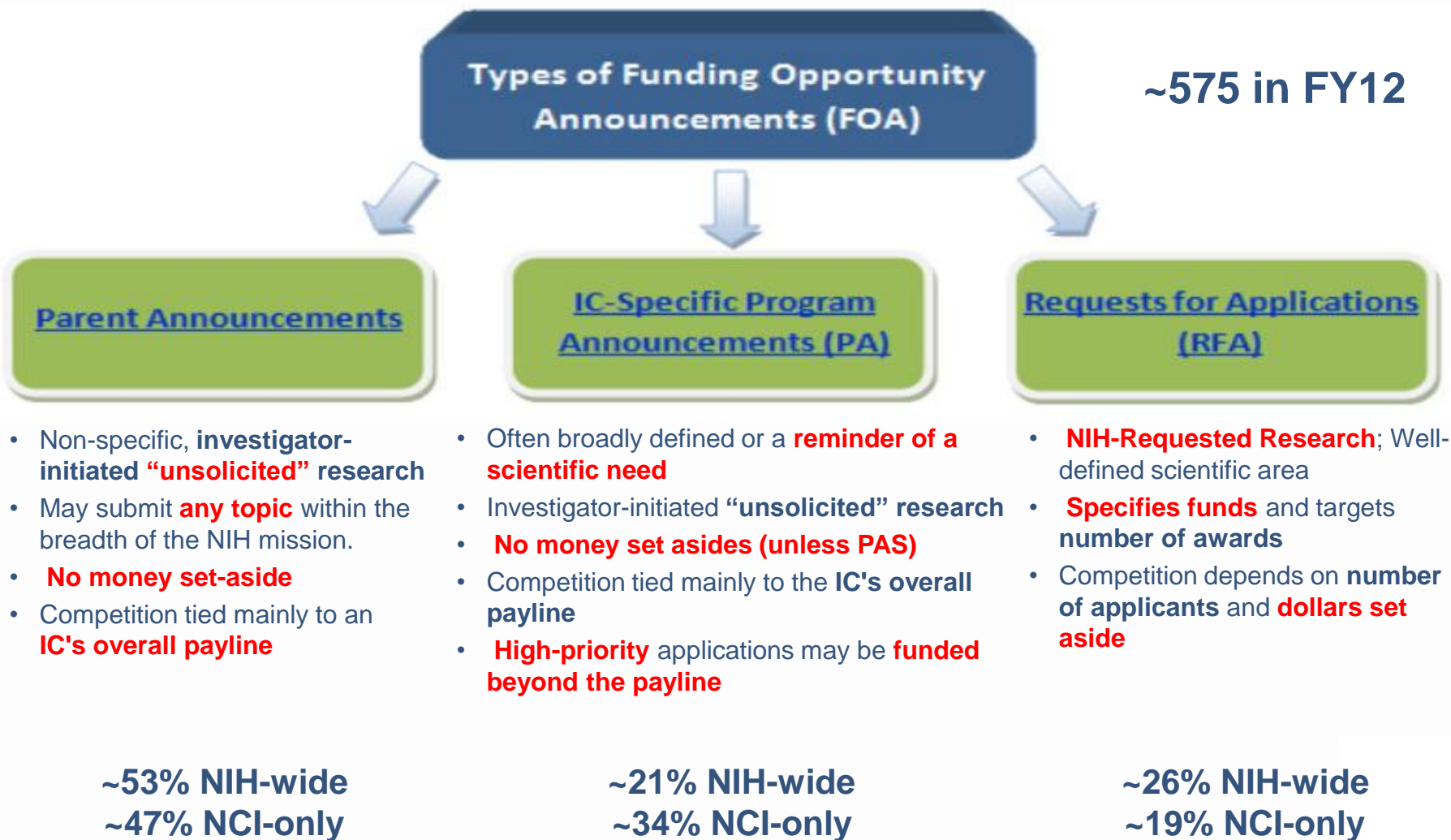
- ~ 76% for extramural support
- ~7,800 grants and contracts

National Institutes of Health (NIH): 27 Institutes and Centers



NIH: Types of Funding Announcements (FOAs)

http://grants.nih.gov/grants/planning_application.htm

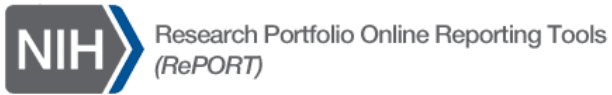


NIH Research Portfolio Online Reporting Tools (RePORT)



U.S. Department of Health & Human Services

Text Size A A A



Search

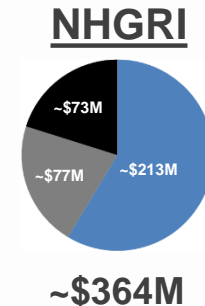
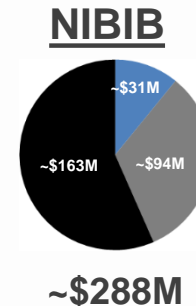
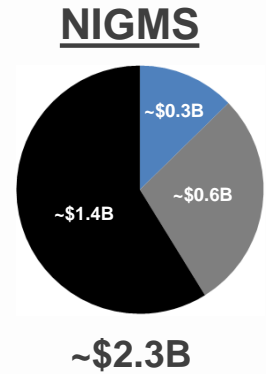
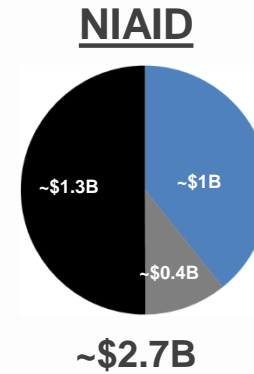
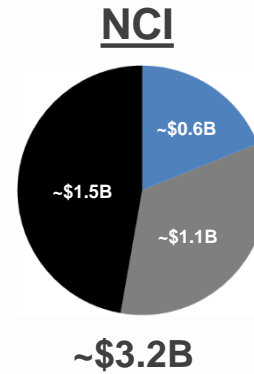
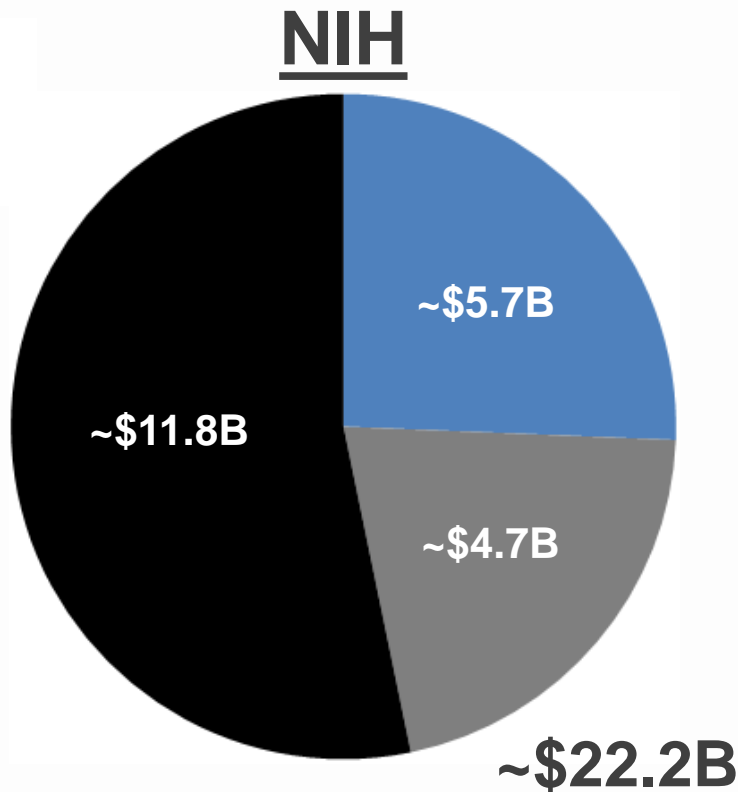
HOME | ABOUT RePORT | FAQs | GLOSSARY | CONTACT US

QUICK LINKS RESEARCH ORGANIZATIONS WORKFORCE FUNDING REPORTS LINKS & DATA

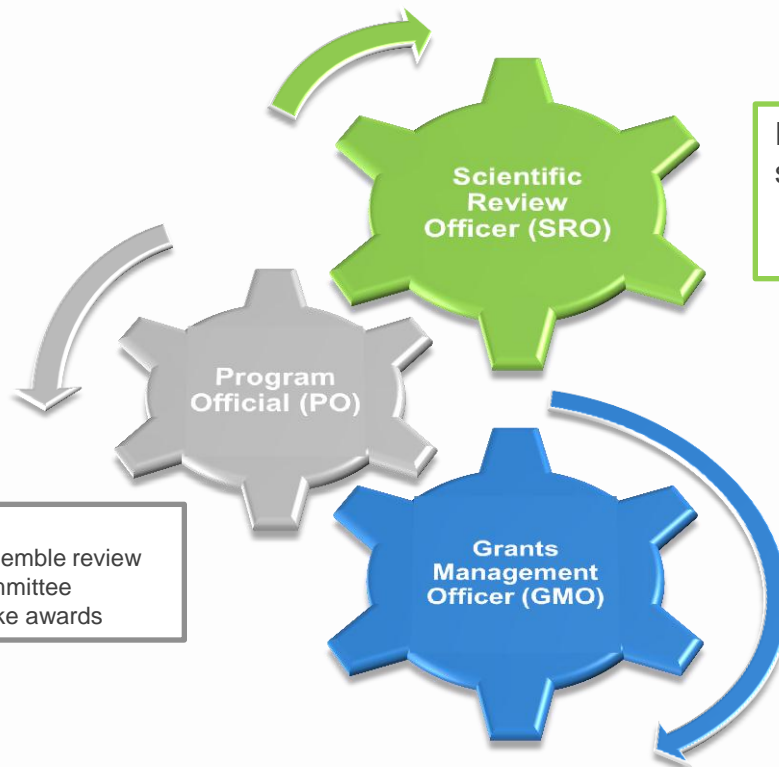
Home > RePORTER > Project Search Results

MyRePORTER Login | Register System Health: GREEN

- RFA
- PA*
- PA



The NIH Extramural Team: Checks & Balances



Ensure **fair** and **unbiased** evaluation of the scientific and technical merit of proposed research

- Manages study sections
- Prepares/issues summary statements

Does not

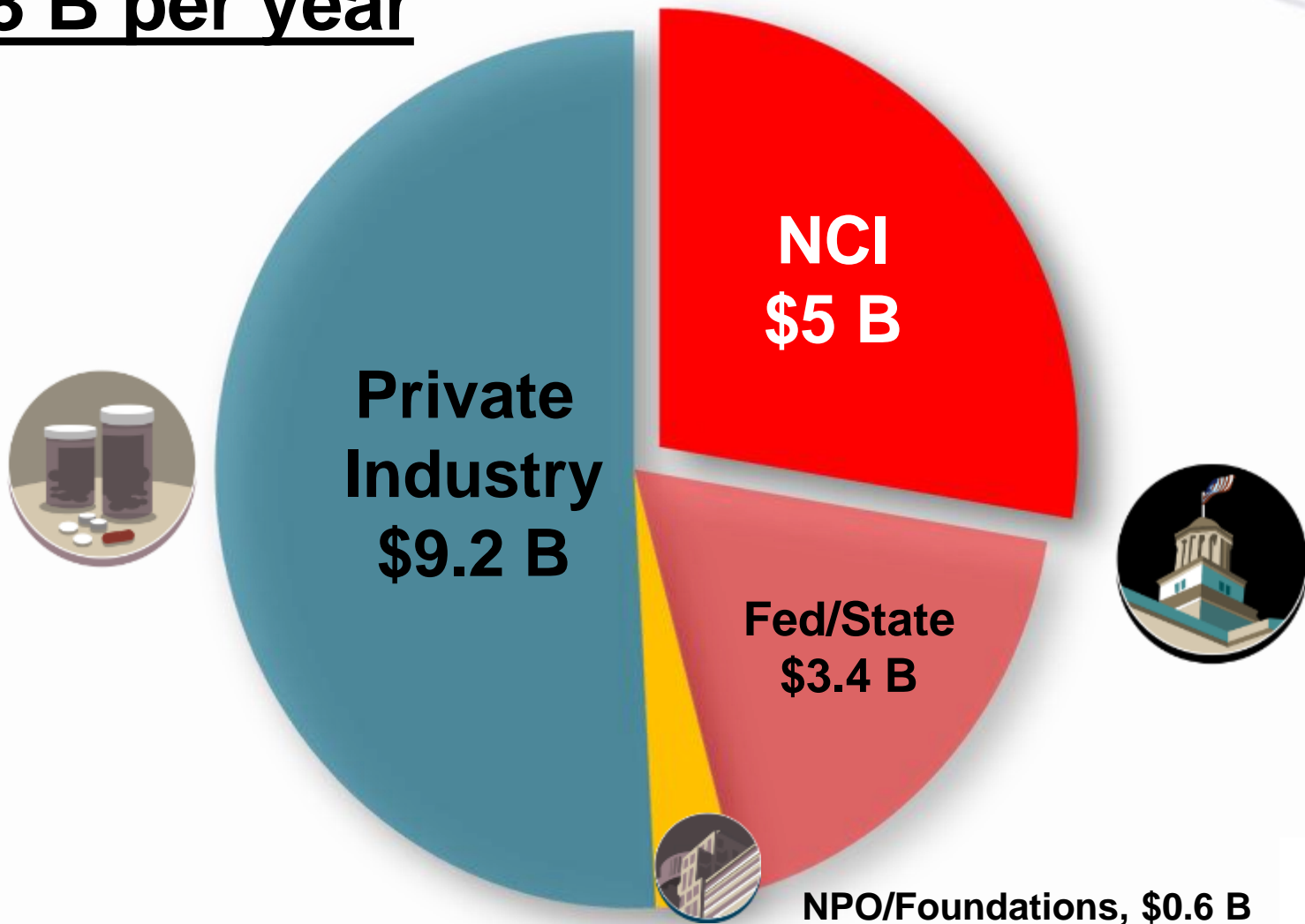
- Assemble review committee
- Make awards

Ensure all required business management actions are performed by the grantee and federal government

- Participates in budget negotiations
- Prepares/issues **Notice of Awards (NoA)**

National Cancer Program: Stakeholders

~\$18 B per year



National Cancer Institute Organization



Director
Harold Varmus, MD

National Cancer Institute

\$5.07B
(FY12)

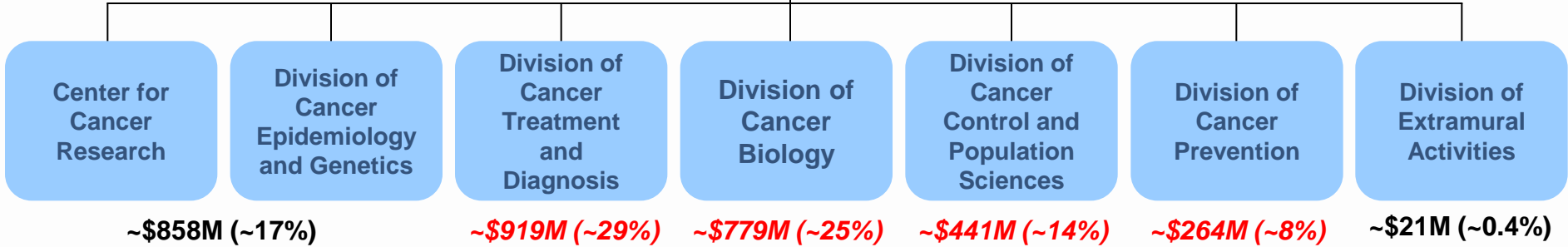


Deputy Director
Douglas Lowy, MD

Office of the Director

CSSI

~\$132 M (~4%)



Conducting – Intramural

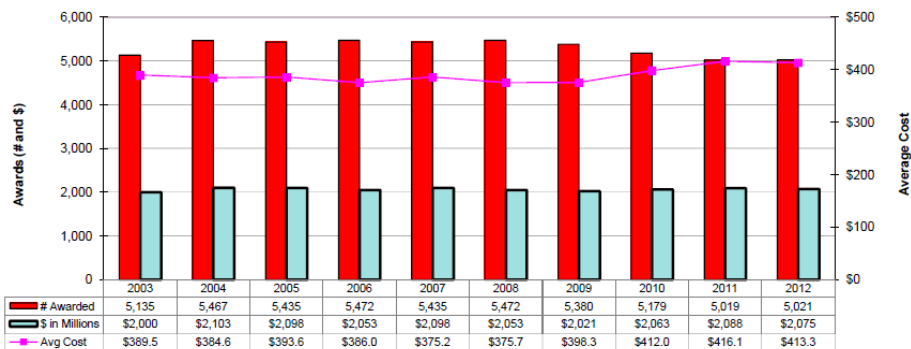
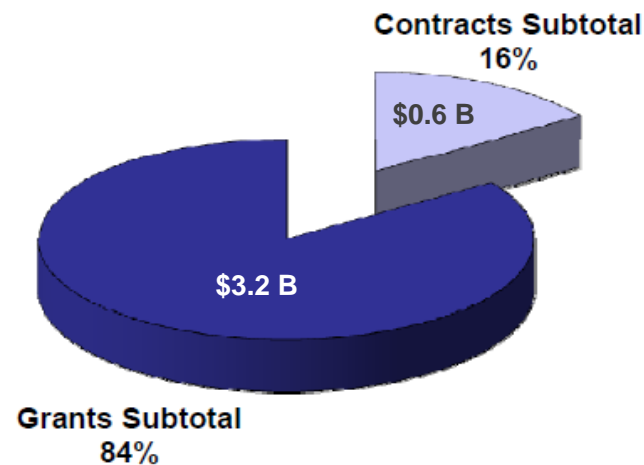
Funding – Extramural

NCI 2012 Fact Book: FY12 Budget Breakdown



Fiscal Year 2012 Budget (Dollars in Thousands)

Mechanism	Amount	Percent
Contracts:		
R&D Contracts	589,715	15.4%
Buildings and Facilities	7,920	0.2%
Construction Contracts	0	0.0%
Subtotal Contracts	597,635	15.6%
Grants:		
Research Project Grants	2,075,295	54.1%
Cancer Centers/Specialized Centers/SPORES	612,789	16.0%
NRSA	65,992	1.7%
Other Research Grants	482,871	12.6%
Construction Grants	0	0.0%
Subtotal Grants	3,236,947	84.4%
Total Extramural Funds	3,834,582	100.0%
Total Intramural/RMS	1,232,760	
*Total NCI	\$5,067,342	



NCI's Federally Funded Research and Development Center (FFRDC)



operated by
Leidos Biomedical Research, Inc.

Frederick National Laboratory
for Cancer Research

Established in 1972 as one of the nation's 39 FFRDC's and the only one devoted exclusively to biomedical research and development

Facts

As one of Frederick County's major employers, the contractor Leidos Biomedical Research Inc. employs approximately 1,800 employees.

Economic Impact

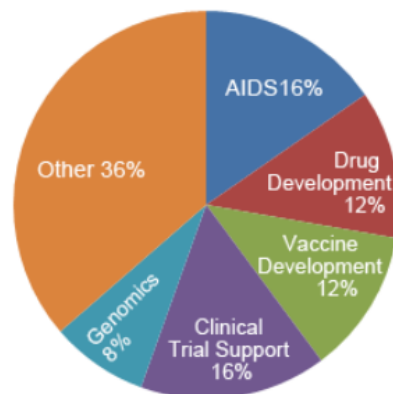
In addition to payroll, Leidos Biomedical Research contributes:

- Dollars spent via Leidos Biomedical Research (formerly SAIC-Frederick) purchase orders, Contract Year 2011
 - Frederick County...\$16,820,351
 - Maryland.....\$183,086,783
- Dollars spent via Leidos Biomedical Research (formerly SAIC-Frederick) purchase orders, 9/26/08–8/10/11
 - Frederick County...\$35,695,585
 - Maryland.....\$286,944,880

Physical

- 68 acres deeded to the Department of Health and Human Services (HHS)
- 991,217 net square feet
- 1,654,035 gross square feet
- 113 buildings on site

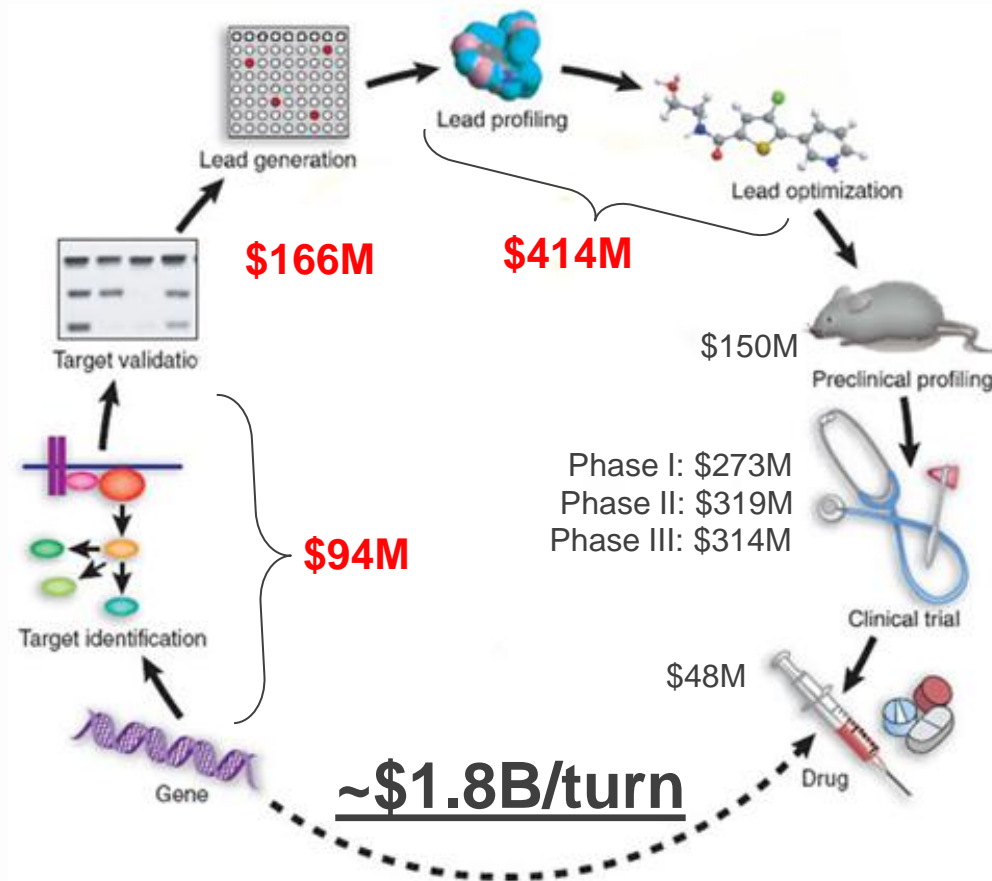
Frederick National Lab Distribution of Effort



NCI Funding in FY12 \$238,204



Translation Pace: How To Break Out of Current Paradigm?



Turning the Crank...

Key Needs (from community '02)

- Standards and protocols
- Real-time, public release of data
- Large, multi-disciplinary teams
- Pilot-friendly team environment to share failures and successes
- Team members with **trans-disciplinary training**

The potential to transform cancer drug discovery and diagnostics

NCI Center for Strategic Scientific Initiatives (CSSI): Concept Shop



Director
Douglas Lowy, MD



~\$190M (FY12)



Deputy Director
Jerry S.H. Lee, PhD

Mission

“...to create and uniquely implement exploratory programs focused on the development and integration of advanced technologies, **trans-disciplinary approaches, infrastructures, and standards**, to accelerate the **creation and broad deployment** of **data, knowledge, and tools** to empower the **entire cancer research continuum** in better understanding and leveraging knowledge of the cancer biology space **for patient benefit...**”



2003, 2007, 2011, 2013



2005, 2010



2008, 2013*



2011



2004, 2008, 2014




2005, 2008



2010

CSSI Programs (FY99-FY14): Diverse Mechanisms

Program	Grants		Cooperative Agreements	Contracts	FFRDC		Interagency Collaborations (Co-funds/joint programs)
	Research	Training			Resource	R&D Subs	
Unconventional Innovations Program				✓			
 INNOVATIVE MOLECULAR ANALYSIS TECHNOLOGIES	✓	✓					
NCI Alliance for Nanotechnology in Cancer	✓	✓	✓		✓	✓	✓   NIST
THE CANCER GENOME ATLAS 		✓	✓	✓		✓	
 CLINICAL PROTEOMIC TUMOR ANALYSIS CONSORTIUM	✓	✓	✓	✓	✓	✓	✓  NIST
BIOSPECIMEN RESEARCH NETWORK						✓	
 Cancer Target Discovery and Development	✓		✓		✓		
PHYSICAL SCIENCES in ONCOLOGY	✓	✓	✓	✓		✓	✓ 
caHUB The Cancer Human Biobank					✓	✓	
Provocative Questions Initiative 	✓						

Support Convergence and Innovation At Many Scales

NCI Alliance for **Nanotechnology** in Cancer

Phase II

Cancer Target Discovery & Development (CTD²)



Early settlers

PHYSICAL SCIENCES in ONCOLOGY



Team Explorers

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Phase II

THE CANCER GENOME ATLAS

Phase II

Provocative Questions Initiative



Discoverers/Pioneers

IMAT
Innovative Molecular Analysis Technologies

Basic

Applied

Translational

Clinical

Industry

Center Framework: “What is Water?” - Measurements → Insights

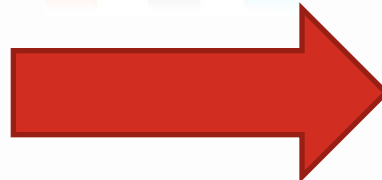
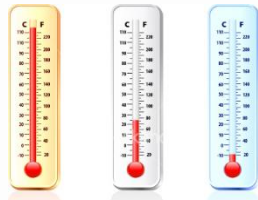


Color (clear, yellow, brown)
Taste (none, metallic, awful)



Phase (liquid, gas, solid)
Phase change (boil, melt, freeze)

Qualitative Descriptions

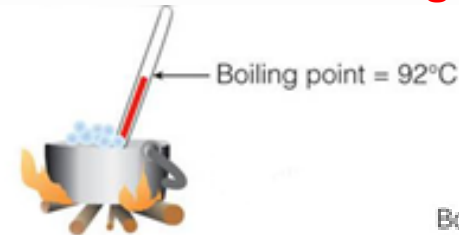


Measurements Taken

Pressure (kg/cm ²)	Temp (°C)	Saturated steam		Superheated steam		
		Vapour enthalpy (kcal/kg)	Specific volume (m ³ /kg)	Density (kg/m ³)	Specific volume (m ³ /kg)	
				at 250°C	at 300°C	
1	99.1	638.8	1.725	0.580	2.454	2.691
2	119.6	646.2	0.902	1.109	1.223	1.542
3	132.9	650.6	0.617	1.621	0.812	0.893
4	142.9	653.7	0.471	2.123	0.607	0.668
5	151.1	656.0	0.382	2.618	0.484	0.533
6	158.1	657.0	0.321	3.115	0.402	0.443
7	164.2	659.5	0.278	3.597	0.343	0.379
8	169.6	660.8	0.245	4.082	0.299	0.331
9	174.5	661.9	0.219	4.566	0.265	0.293
10	179.1	662.9	0.198	5.051	0.238	0.263
12	187.1	664.5	0.166	6.024	0.196	0.218
14	194.1	665.7	0.143	6.993	0.167	0.186
16	200.4	666.7	0.126	7.937	0.145	0.162
18	206.1	667.4	0.112	8.929	0.128	0.143
20	211.4	668.0	0.101	9.901	0.114	0.128
22	216.2	668.4	0.092	10.870	0.103	0.116
24	220.7	668.7	0.085	11.765	0.093	0.106
26	225.0	669.0	0.078	12.821	0.085	0.097
28	229.0	669.1	0.073	13.699	0.078	0.089
30	232.7	669.2	0.068	14.706	0.072	0.083

LOTS of Quantitative “Data”

But also LOTS of disagreements...

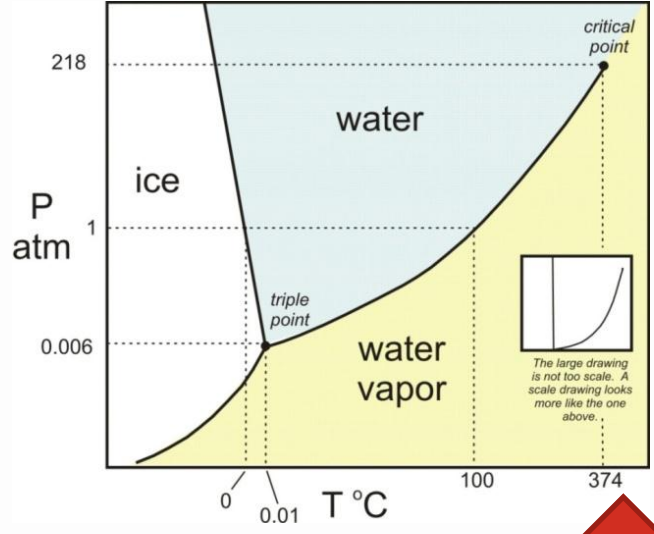
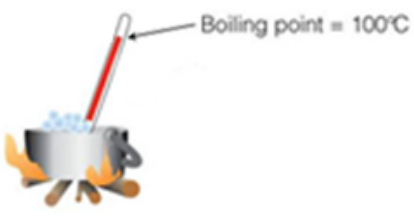
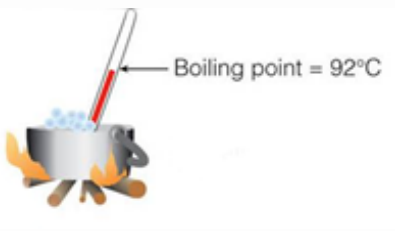


Boiling point = 100°C



Standards and Sharing of Data → New Insights and Understanding

- Define samples & protocols
- Share collected data



New Understanding

- Phase boundaries
 - V/L equilibrium
- Triple Point

(Phase Diagram)

New Parameter
“Pressure”



Pressure (kg/cm ²)	Temp (°C)	Saturated steam		Superheated steam		
		Vapour enthalpy (kcal/kg)	Specific volume (m ³ /kg)	Density (kg/m ³)	Specific volume (m ³ /kg)	
			at 250°C		at 300°C	
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4	142.9	653.7	0.471	2.123	0.607	0.668
5	151.1	656.0	0.382	2.618	0.484	0.533
6	158.1	657.0	0.321	3.115	0.402	0.443
7	164.2	659.5	0.278	3.597	0.343	0.379
8	169.6	660.8	0.245	4.082	0.299	0.331
9	174.5	661.9	0.219	4.566	0.265	0.293
10	179.1	662.9	0.198	5.051	0.238	0.263
12	187.1	664.5	0.166	6.024	0.196	0.218
14	194.1	665.7	0.143	6.993	0.167	0.186
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LOTS of
Quantitative
and
Reproducible
Data

(Steam Table)

2003 Launch of the Technology Dashboard of CSSI: IMAT



INNOVATIVE MOLECULAR
ANALYSIS TECHNOLOGIES

To support the **development, maturation, and dissemination** of **innovative and/or potentially transformative next-generation technologies**

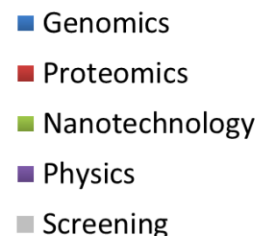
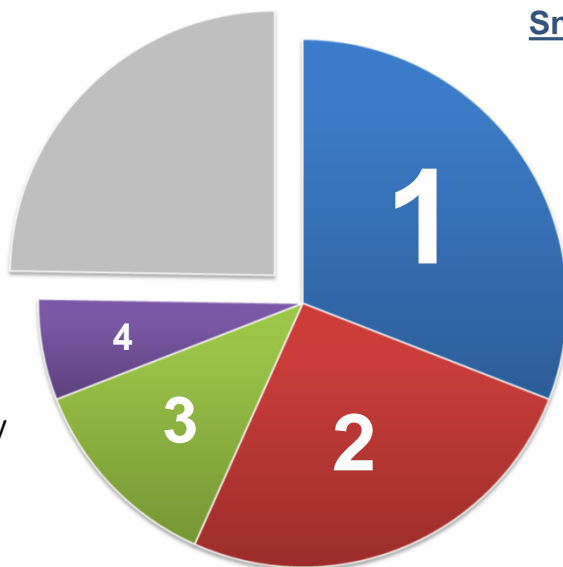
Innovative Technologies for Molecular Analysis of Cancer

- Proof-of-concept technologies/projects encouraged
- Milestone and technology development driven (no biology)

Application of Emerging Technologies for Cancer Research

- Validation and dissemination of platforms
- Demonstration of impact on basic and clinical research

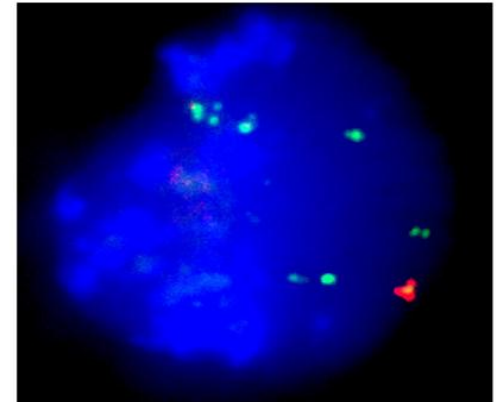
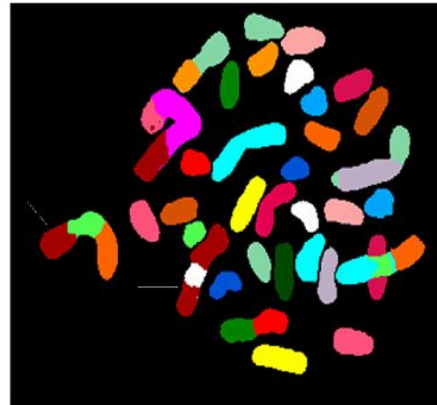
Snapshot of Initial Applications (2003-2004)



First Step(back)- Cancer Genomics: Taking a Page from Engineers

Disease of Genomic Alterations

- Copy number
- Expression (regulation of)
- Regulation of translation
- Mutations
- Epigenome



- **Systematic identification of all genomic changes**
- **Repeat (a lot) for individual cancer**
- **Repeat for many cancers**
- **Make it publically available**

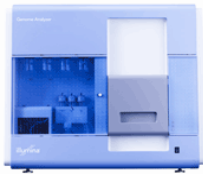
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Steam table (Reference)

Many "Thermometers": Heterogeneity of Platforms



454



Illumina

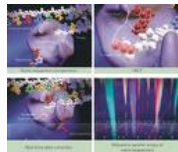


SOLiD

Complete Genomics
Complete Genomics



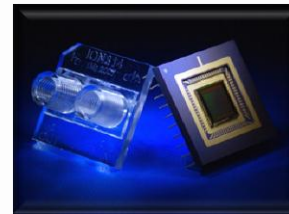
Helicos



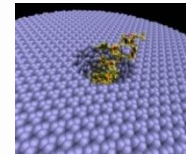
Visigen



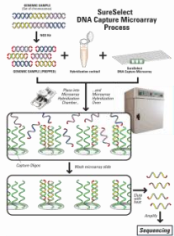
PacBio



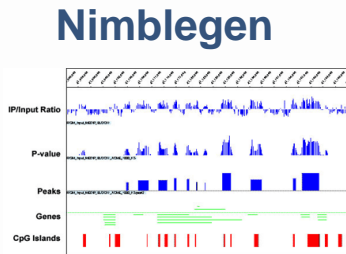
Ion-Torrent



Oxford Molecular



Agilent

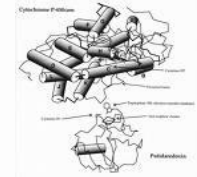


Nimblegen



LaserGen

ZSGenetics



NABsys

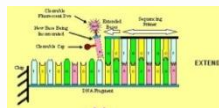


Raindance



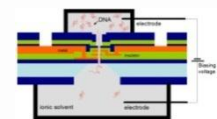
Febit

Intelligent Biosystems

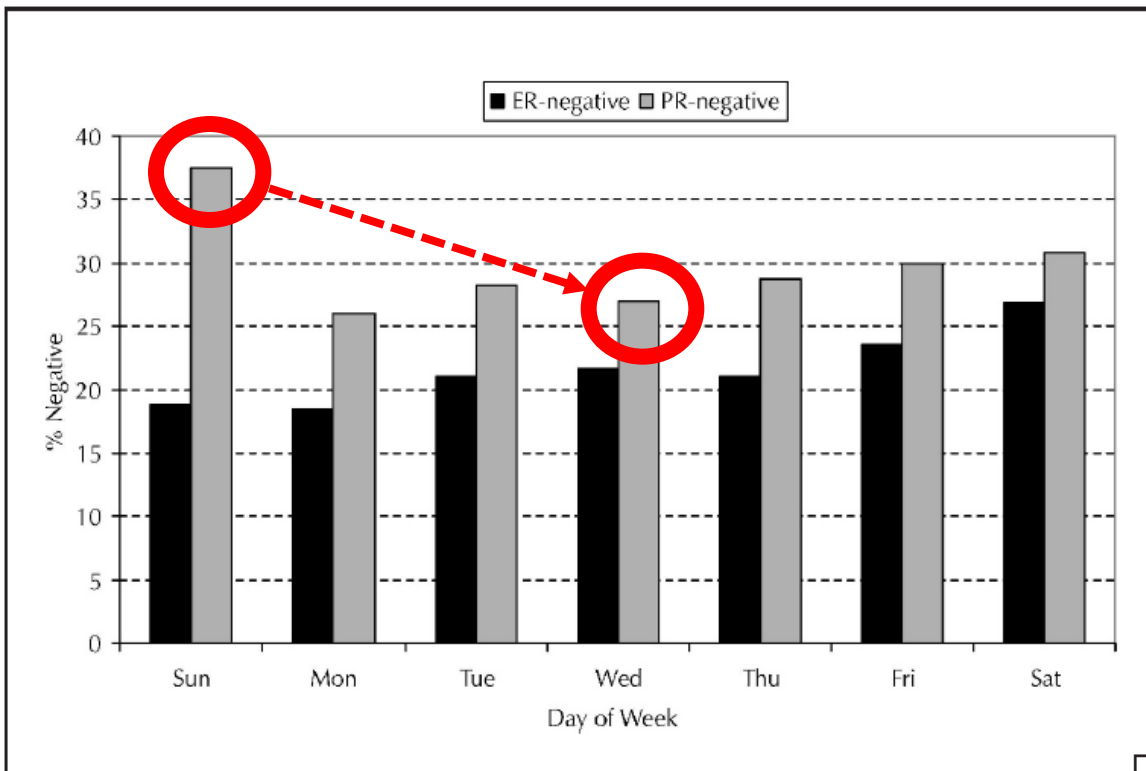


Halycon

IBM



Getting “Water” Right: Samples AND Handling Matter!



caHUB The Cancer Human Biobank

“Garbage In...Garbage Out”

“...We found that specimens **obtained late in the week** (prolonged specimen handling) are **more likely to be ER/PR negative** than specimens **obtained on other weekdays** (regular specimen handling)...”

Table 1. Frequency of Specimen Removal by Day of the Week

Day	Cases	ER-Negative	PR-Negative
Sunday	16	3	6
Monday	1252	230	325
Tuesday	1176	248	332
Wednesday	784	170	212
Thursday	904	191	259
Friday	919	216	276
Saturday	26	7	8
System	5077	1065	1418

Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

TCGA: Connecting Multiple Standardized Sources, Experiments, and Data Types

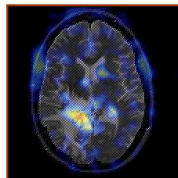
THE CANCER GENOME ATLAS



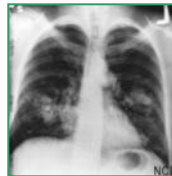
Three Cancers- Pilot

Multiple data types

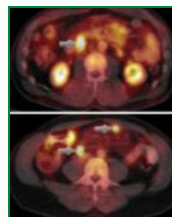
**glioblastoma multiforme
(brain)**



**squamous carcinoma
(lung)**



**serous
cystadenocarcinoma
(ovarian)**



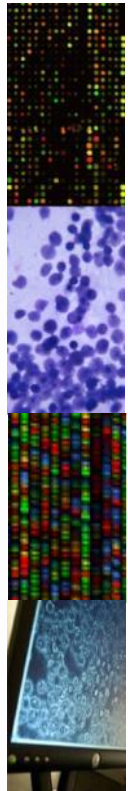
Biospecimen Core
Resource with more
than 13 Tissue
Source Sites

7 Cancer Genomic
Characterization
Centers

3 Genome
Sequencing
Centers

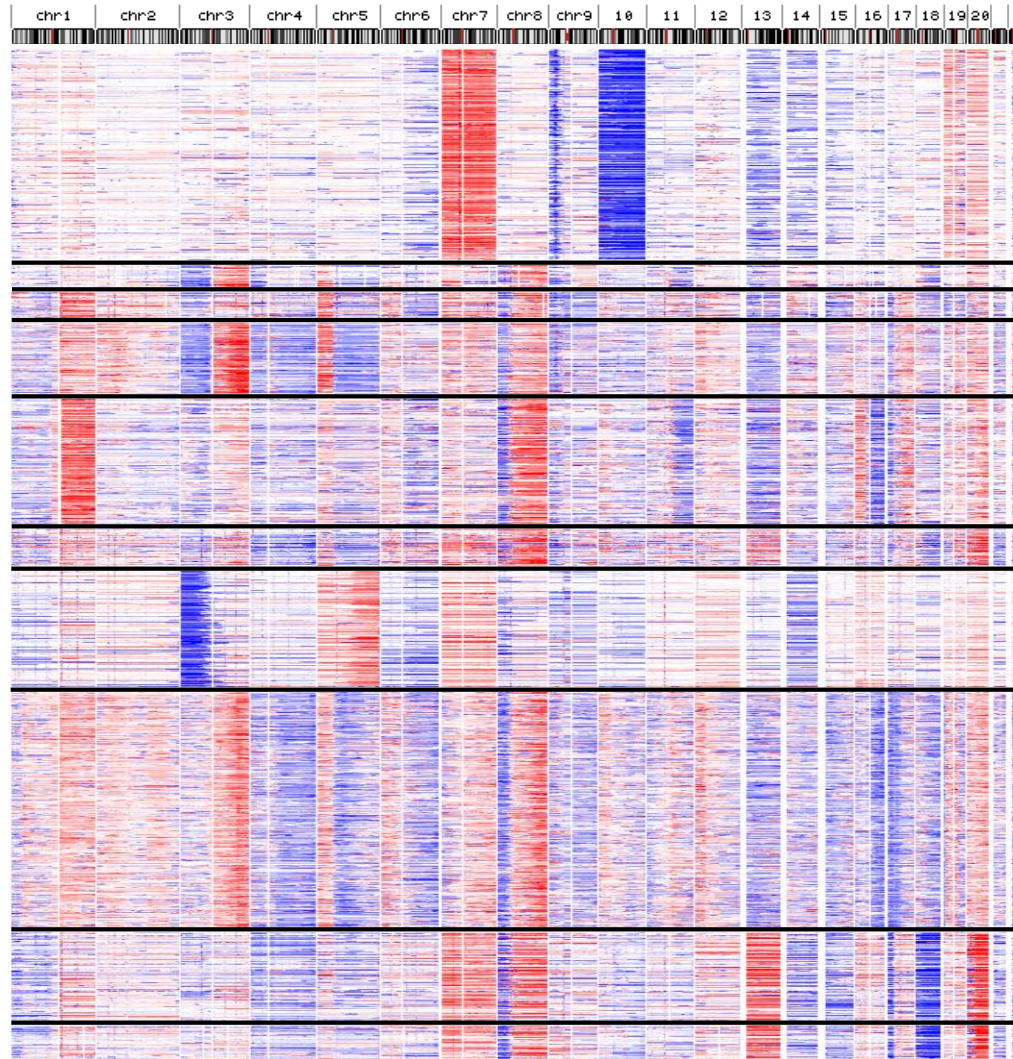
Data Coordinating
Center

- Clinical diagnosis
- Treatment history
- Histologic diagnosis
- Pathologic status
- Tissue anatomic site
- Surgical history
- Gene expression
- Chromosomal copy number
- Loss of heterozygosity
- Methylation patterns
- miRNA expression
- DNA sequence



Genomic “Steam Table”

Summer 2011

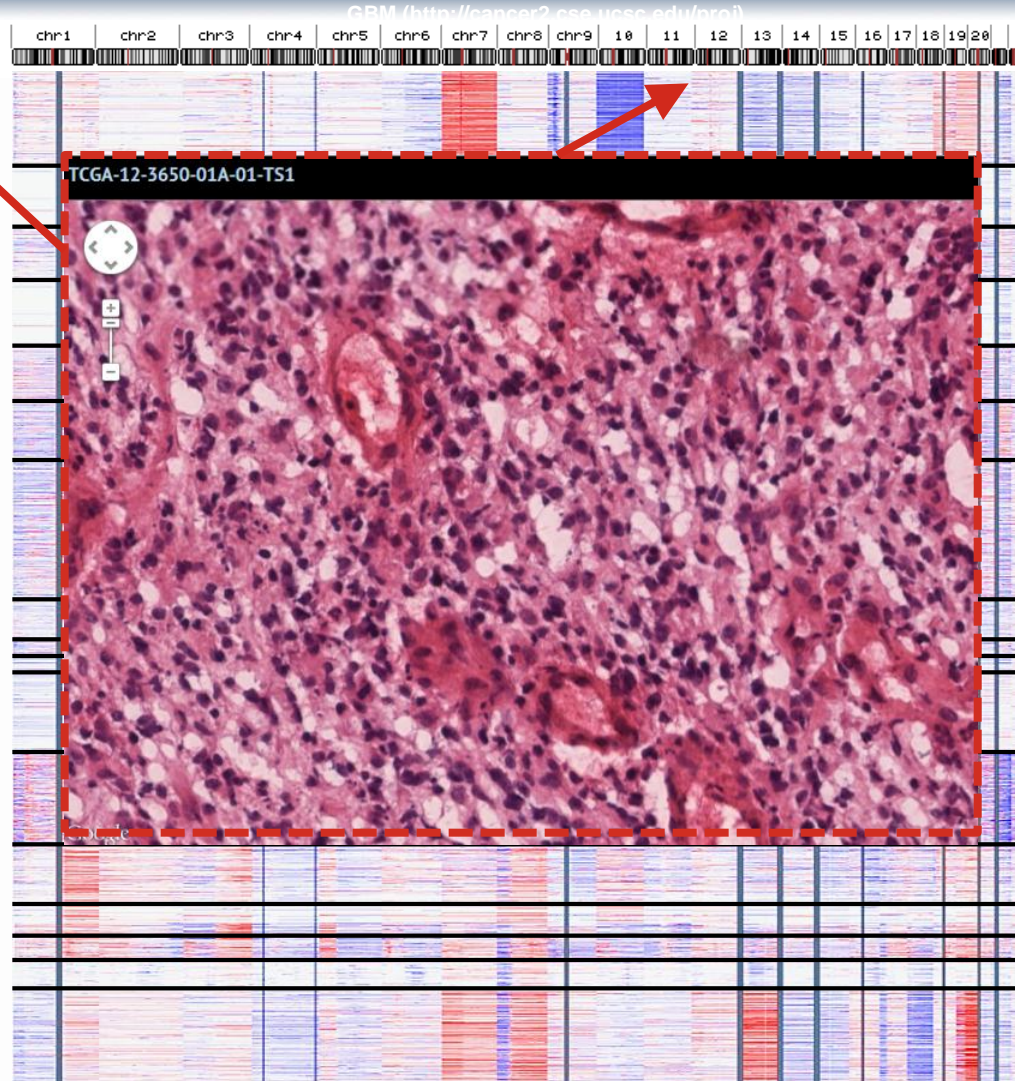
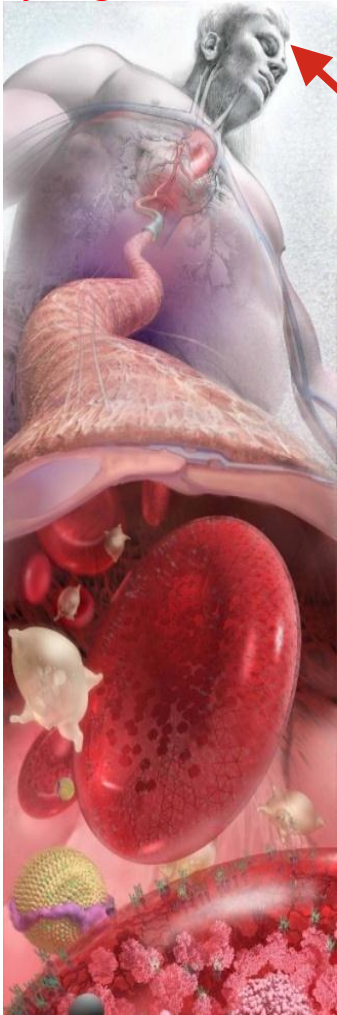


Glioblastoma:	470
Head & neck:	51
Lung adeno:	57
Lung squamous:	159
Breast carcinoma:	180
Stomach adeno:	84
Kidney clear carc:	260
Ovarian serous:	520
Colon adeno:	198
Rectum carcinoma:	74

Total: 2053

Genomic “Steam Table”

Spring 2013

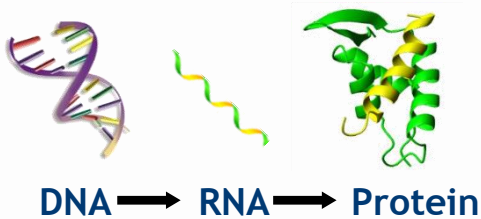


Glioblastoma:	563
Brain lower grade glioma:	180
Head & neck:	306
Thyroid carc:	401
Lung adeno:	356
Lung squamous:	343
Breast carc:	866
Stomach adeno:	237
Liver hep. carc:	97
Kidney pap. cell carc:	103
Kidney clear cell carc:	493
Ovarian serous:	559
Uterine corpus end. carc:	492
Cervical carc:	102
Bladder carc:	135
Prostate adeno:	171
Colon/rectum adeno:	575

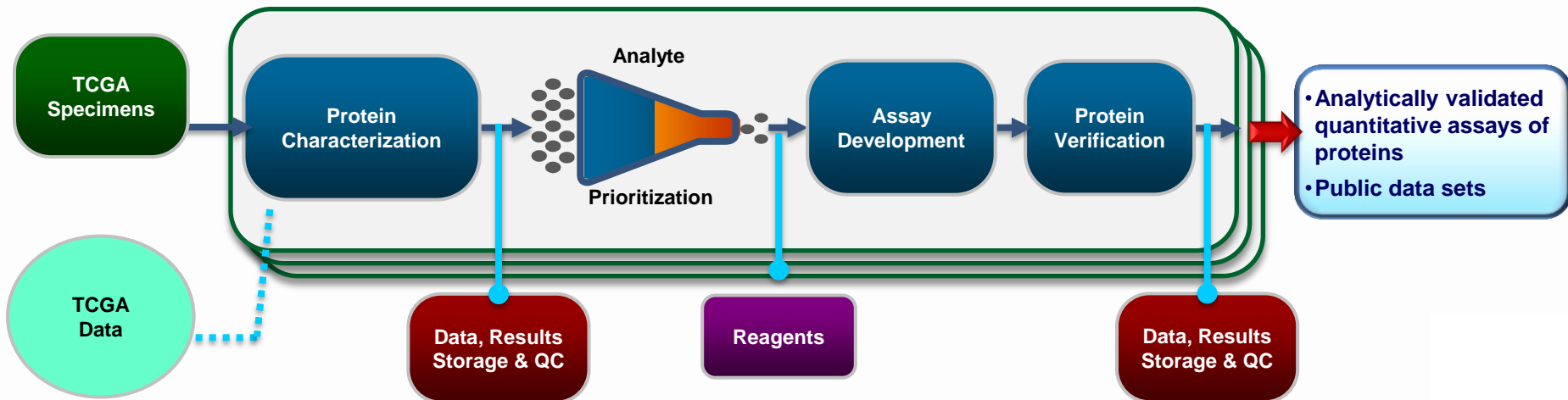
Total: 5979

Clinical Proteomic Tumor Analysis Consortium (CPTAC)

Phase II Launched Sept 2011



- Analyze matched TCGA samples using two approaches
 - Targeting genome to proteome
 - Mapping proteome to genome
- Develop **validated and quantitative** assays and reagents
 - Lessons from Phase I (mock 510K submission)
 - Antibody Characterization Lab
- Distribute raw and analyzed data via public data portal



CPTAC Public Resources:

http://proteomics.cancer.gov



LIVE

CPTAC Data Portal

11,419 files (2.2 TB)

LIVE

NCI Antibody Portal

280 mAbs (~\$35)

COMING SOON

CPTAC Assay Portal

542 assays

CPTAC, TCGA Cancer Proteome Study of Colorectal Tissue
 Embargo Release Date: December 04, 2014

The goal of the CPTAC, TCGA Cancer Proteome Study of Colorectal Tissue is to analyze the proteomes of TCGA tumor samples that have been comprehensively characterized by molecular methods (Cancer Genome Atlas Network, Nature 2012).

Data Sets

Name	Size
CPTAC_TCGA_Colorectal_Cancer_Protocols_and_Clinical_Data	839KB
TCGA-AA-3807-O1A-22_Proteome_VU_20121019	80B
TCGA-AA-3808-O1A-22_Proteome_VU_20121205	90B
TCGA-AA-3810-O1A-22_Proteome_VU_20121029	80B
TCGA-AA-3518-O1A-11_Proteome_VU_20120915	80B
TCGA-AA-3525-O1A-11_Proteome_VU_20121209	80B
TCGA-AA-3526-O1A-11_Proteome_VU_20130106	80B
TCGA-AA-3529-O1A-12_Proteome_VU_20121203	90B
TCGA-AA-9331-O1A-22_Proteome_VU_20130101	80B
TCGA-AA-3534-O1A-22_Proteome_VU_20130208	70B
TCGA-AA-3552-O1A-22_Proteome_VU_20130125	80B
TCGA-AA-3554-O1A-22_Proteome_VU_20121122	80B
TCGA-AA-3807-O1A-22_Proteome_VU_20121019	80B
TCGA-AA-3808-O1A-22_Proteome_VU_20121205	90B

Antibody Portal

Antigen Recognition: show 25 entries, Showing 1 to 231 of 231 entries

Antibodies	Antigens	Purchase
<input type="checkbox"/> OPTC-ARX1B1-1	Aldo-keto Reductase Family 1 Member B1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-ARX1B1-2	Aldo-keto Reductase Family 1 Member B1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-ARX1B1-3	Aldo-keto Reductase Family 1 Member B1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-ARX1B1-4	Aldo-keto Reductase Family 1 Member C1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-ARX1C1-1	Aldo-keto reductase family 1 member C1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-ARX1C1-2	Aldo-keto reductase family 1 member C2	<input type="checkbox"/>
<input type="checkbox"/> OPTC-ARX1C1-3	Aldo-keto reductase family 1 member C2	<input type="checkbox"/>
<input type="checkbox"/> OPTC-ARX1C1-4	Aldo-keto reductase family 1 member C2	<input type="checkbox"/>
<input type="checkbox"/> OPTC-ARX1A1-1	Annexin A1 (Annexin I)	<input type="checkbox"/>
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<input type="checkbox"/> OPTC-ARX1A1-3	Annexin A1 (Annexin I)	<input type="checkbox"/>
<input type="checkbox"/> OPTC-APFK1-2	APEX Nuclease 1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-BC2L1-1	BC2 Like 1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-BC2L1-2	BC2 Like 1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-BC2L1-3	BC2 Like 1	<input type="checkbox"/>
<input type="checkbox"/> OPTC-BC2L1-4	BC2 Like 2	<input type="checkbox"/>
<input type="checkbox"/> OPTC-BC2L1-5	BC2 Like 2	<input type="checkbox"/>
<input type="checkbox"/> OPTC-BC2L1-6	BC2 Like 2	<input type="checkbox"/>
<input type="checkbox"/> OPTC-CAR-1	Carboxyl dehydratase VIII	<input type="checkbox"/>
<input type="checkbox"/> OPTC-CAR-2	Carboxyl dehydratase VIII	<input type="checkbox"/>
<input type="checkbox"/> OPTC-Calyd-1	Calyculin Receptor Associated Protein 4	<input type="checkbox"/>
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<input type="checkbox"/> OPTC-Calyd-3	Calyculin Receptor Associated Protein	<input type="checkbox"/>
<input type="checkbox"/> OPTC-CDC4		<input type="checkbox"/>

Protein Details: OPTC-ARX1B1-1

Antibody: OPTC-ARX1B1-1

Antigen: Aldo-keto Reductase Family 1 Member B1

Accession: P08288

Function: Aldo-keto reductase family 1 member B1

EC: 1.1.1.1

Gene: AKR1B1

Protein Structure:

Sequence:

References:

Assay Portal

Search the Assay Database by:

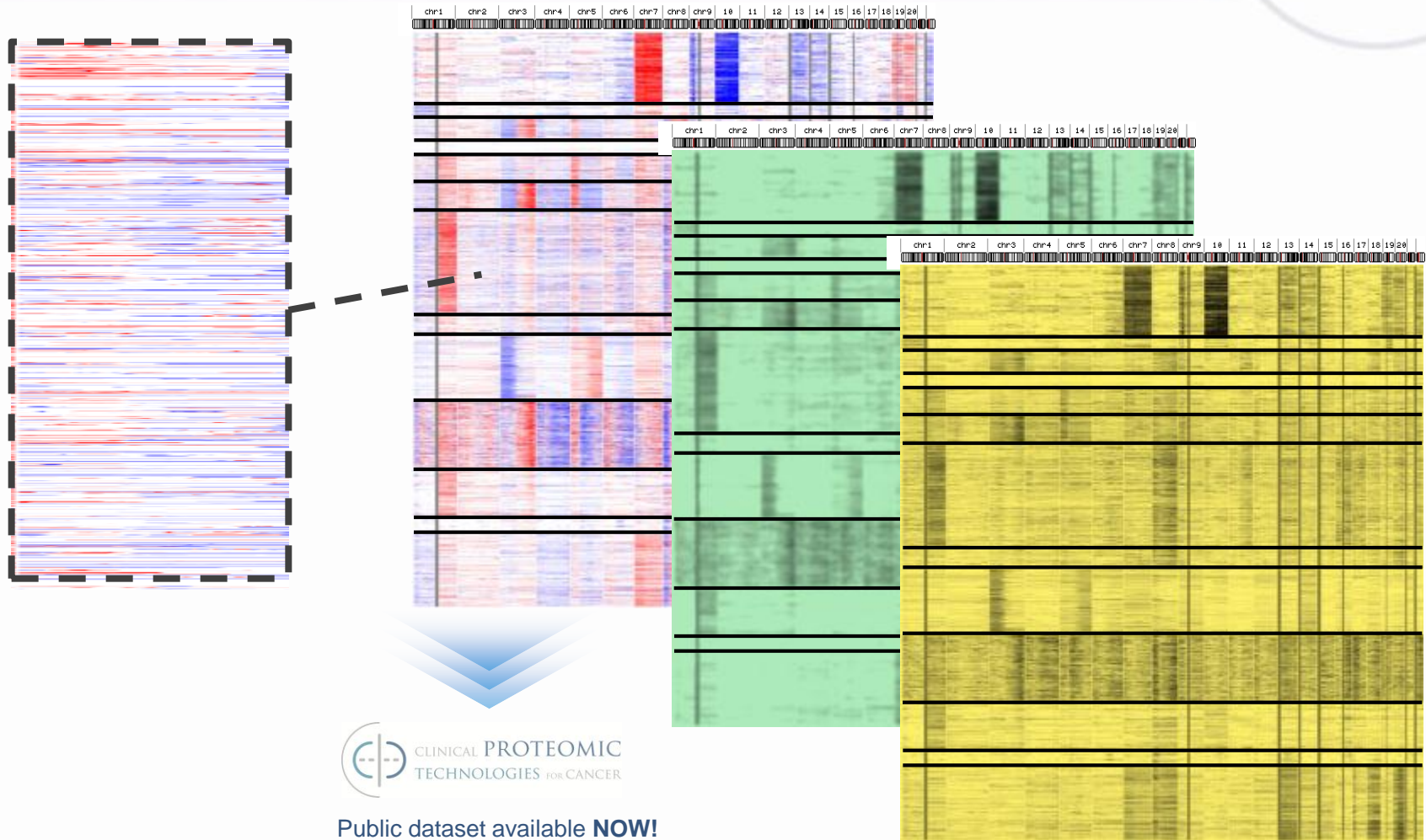
Search: Showing 1 to 50 of 870 entries

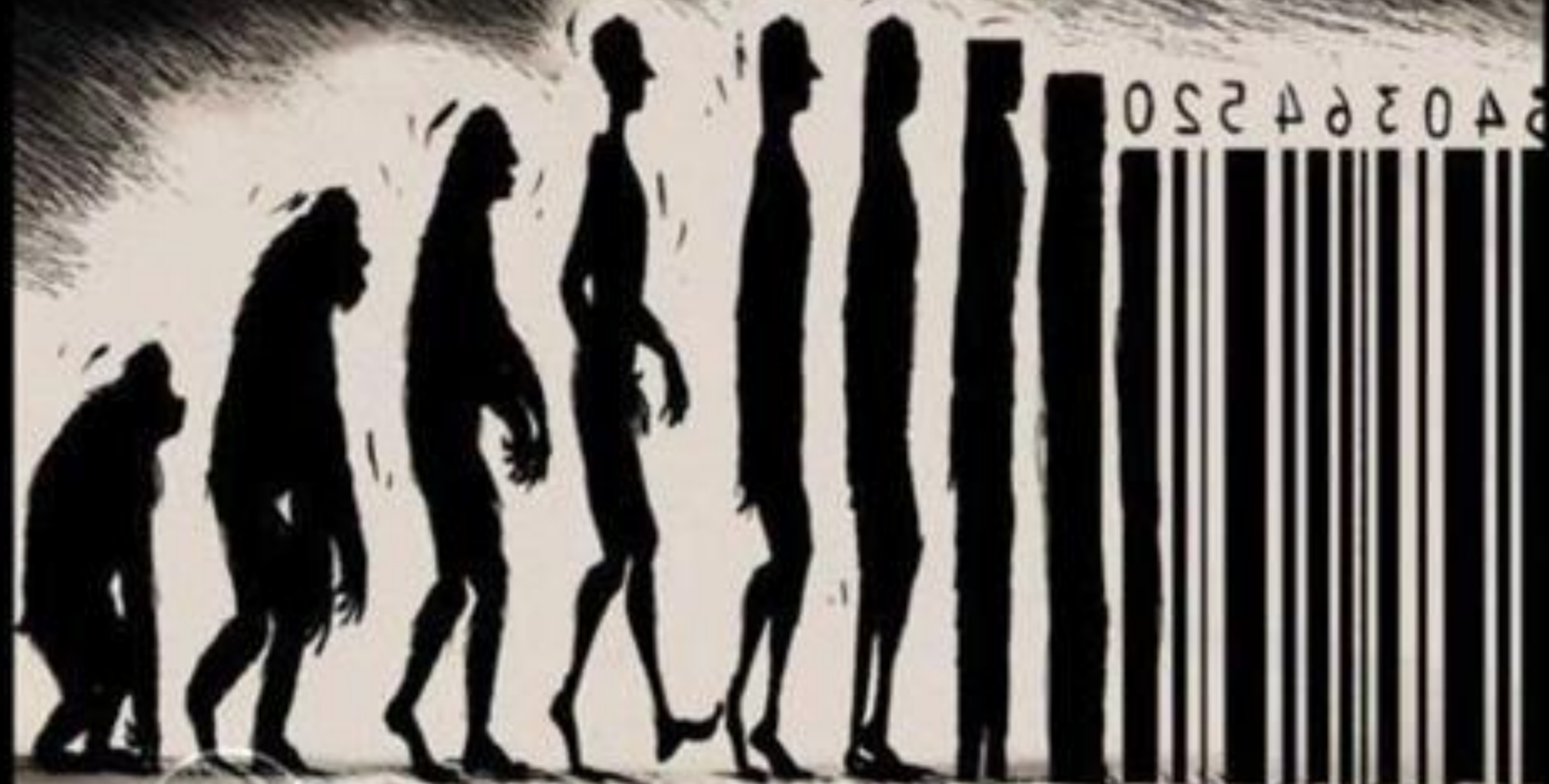
Proteins and peptides for which assays are available	Submitting Laboratory	Modification	Assay Type	Matrix
AARS - UniProt Accession ID: P49588				
AVDETFPPVPR	Fred Hutchinson Cancer Research Center	unmodified	direct MRM	cell line lysate pool
TIVLADGGPPDPR	Fred Hutchinson Cancer Research Center	unmodified	direct MRM	cell line lysate pool
ABAT - UniProt Accession ID: P28044				
ALLTQLDQAR	Fred Hutchinson Cancer Research Center	unmodified	direct MRM	cell line lysate pool
QTCFDFPDDSR	Fred Hutchinson Cancer Research Center	unmodified	direct MRM	cell line lysate pool
ABCD3 - UniProt Accession ID: P28288				
VLQELWLPQGR	Seoul National University / Korea Institute of Science and Technology	unmodified	direct MRM	cell line lysate pool
VLQELWLPQGR	Fred Hutchinson Cancer Research Center	unmodified	direct MRM	cell line lysate pool

Release Date	Disease	# of Samples
9/4/2013	Colorectal	95
2/20/2014	Breast	105
4/2014	Ovarian	TBD

~8,000 proteins
~12,000 phospho-proteins

Where Do We Go From Here? Is it JUST More Data?





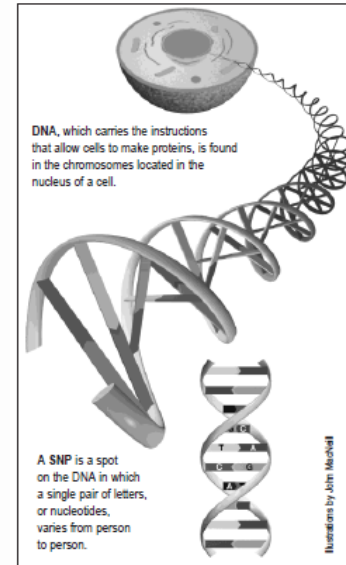
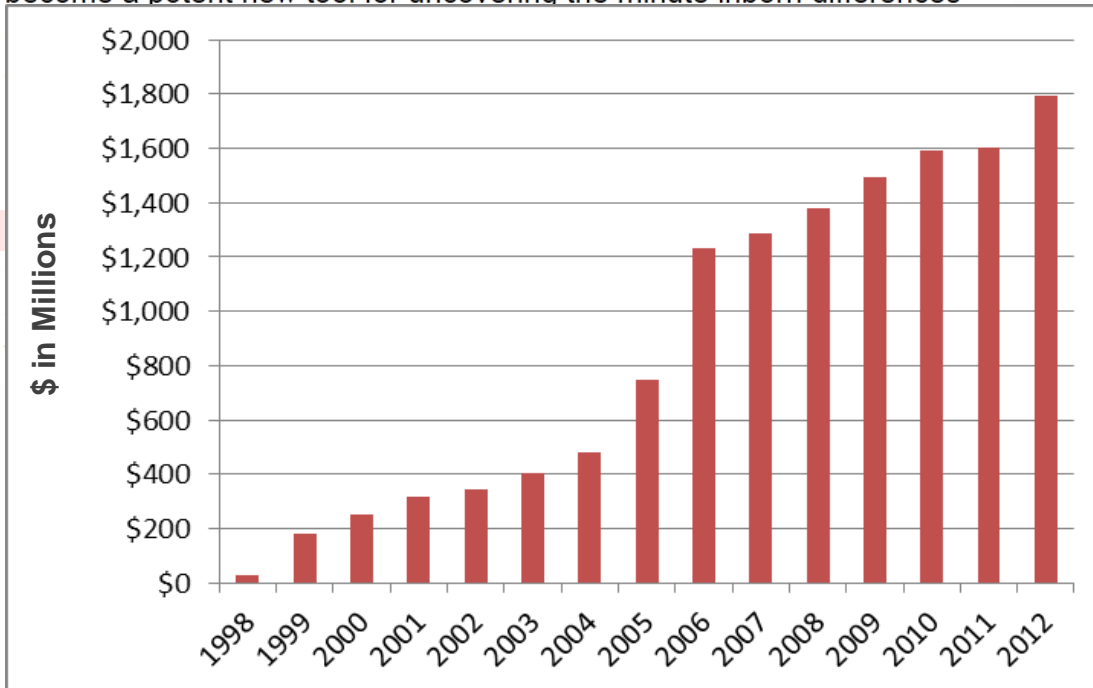
Personalized Medicine

THE WALL STREET JOURNAL.

Friday, April 16, 1999

The pharmaceutical industry makes billions of dollars a year selling one-size-fits-all medicines. But now the race is on to come up with tailor-made drugs that will treat people based on their individual genetic makeup.

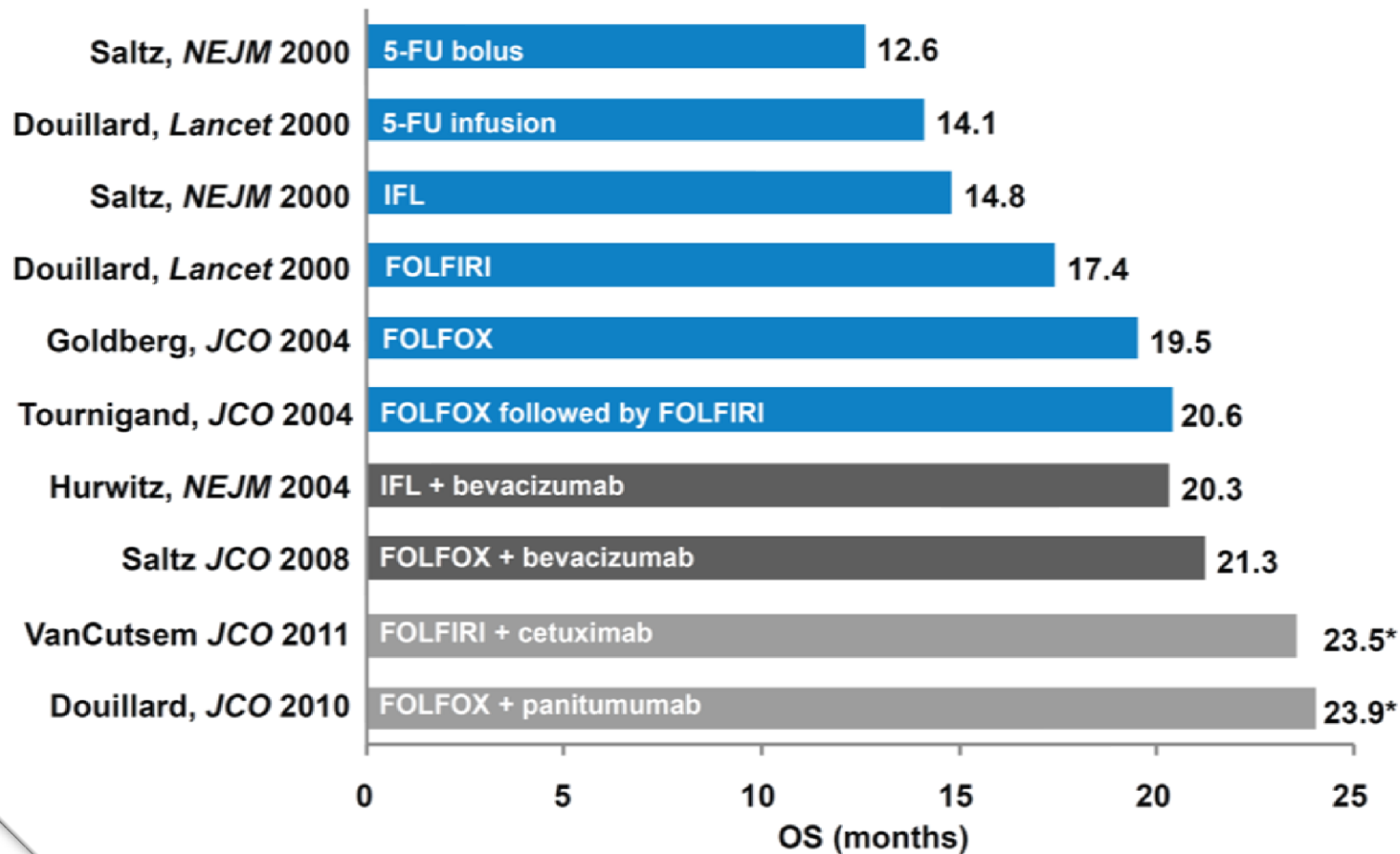
Drug companies hope to create a map of genetic landmarks that will become a potent new tool for uncovering the minute inborn differences



How Fine-Tuning By Drug Makers Will Work

- **Herceptin from Genentech Inc.**
Breast-cancer drug developed specifically to treat a minority of patients whose tumors have elevated levels of a protein, her-2.
- **Xeloda from Roche Holding Ltd.**
Some patients may respond better to this breast-cancer drug than others because of differences in enzymes that process it.
- **Clozaril from Novartis AG**
Old schizophrenia drug that causes rare blood disorder in a small number of patients; researchers hope to use gene-map data to develop test to predict who will get the disorder.
- **Orzel from Bristol-Myers Squibb Co.**
Colorectal cancer drug currently under FDA review; company is performing studies to identify which patients are more likely to develop diarrhea and other side-effects from the drug.

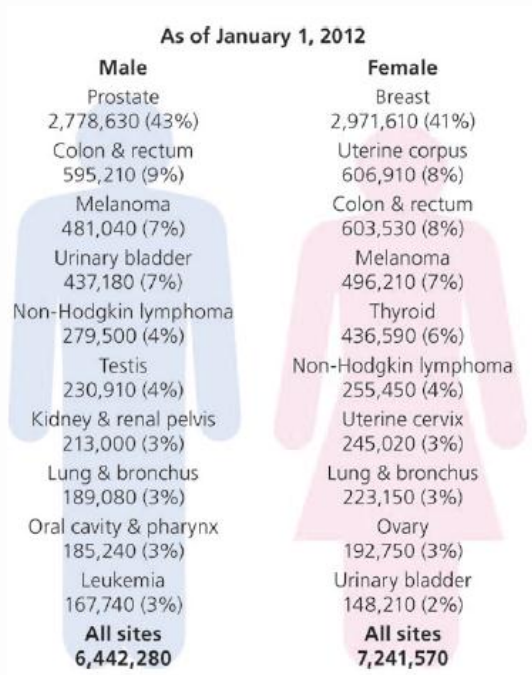
Incremental Improvements Have Doubled Overall Survival in the Last Decade



*KRAS wild-type population

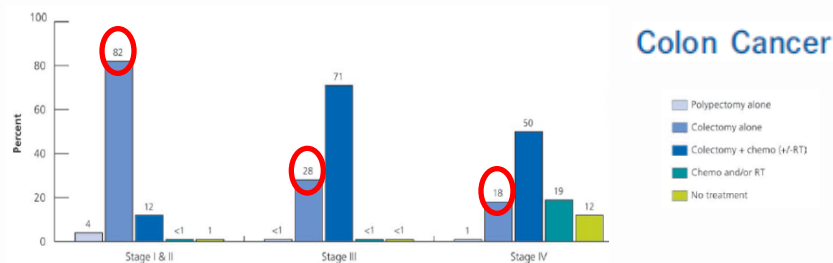
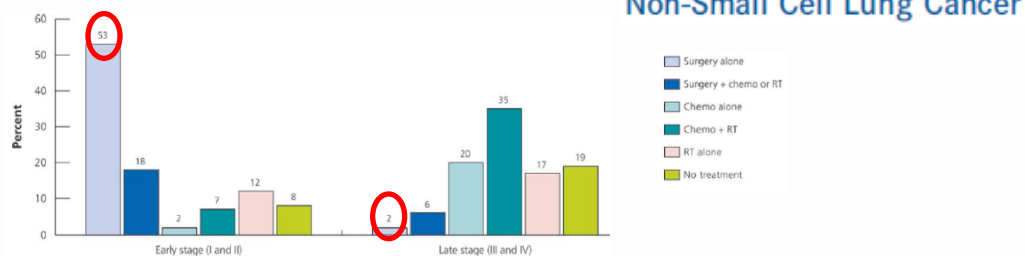
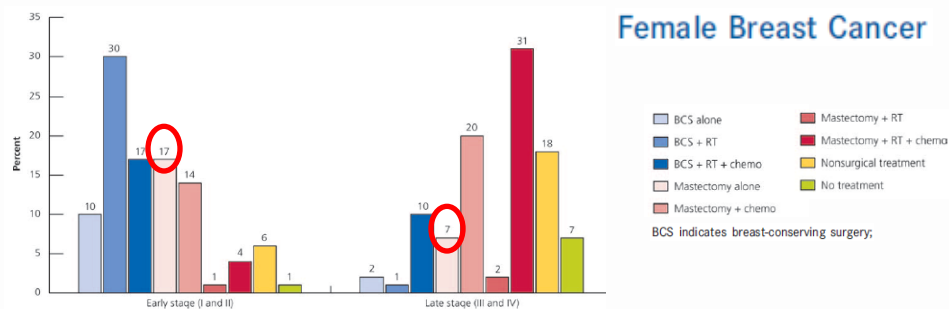
2012: Cancer Treatment and Survivorship Statistics

An estimated 13.7 million Americans with a history of cancer were alive on January 1, 2012.



Estimated Numbers of US Cancer Survivors by Site.

Cancer Treatment Patterns by Stage, 2008.



Provocative Question (PQ) Project: Seeding Innovations for the Future



nature

NATURE | COMMENT

Nature Jan 26, 2012

Science funding: Provocative questions in cancer research

Harold Varmus & Ed Harlow



- **Goal:**
 - Challenge the scientific community to creatively think about and answer **important, but non-obvious or understudied**, provocative questions (PQs) in cancer research
- **Implementation:**
 - PQs solicited through website and workshops
 - **Phase 1:** requested R01/R21 applications on 24 final PQs (**55 awards**)
 - **Phase 2:** new set of 24 PQs for R01/R21 apps (**93 awards**)
 - **Phase 3:** new set of 20 PQs

PQA4: For tumors that arise from a pre-malignant field, what properties of cells in this field can be used to design strategies to inhibit the development of future tumors?

PQC4: What in vivo imaging methods can be developed to portray the "cytotype" of a tumor?

PQD1: What molecular properties make some cancers curable with conventional chemotherapy?

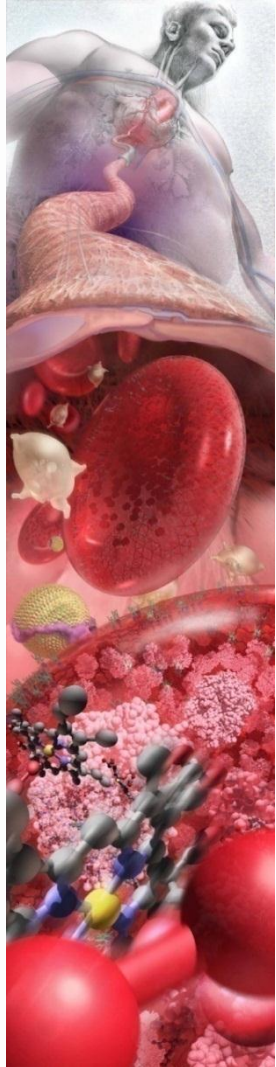
PQB1: Why do second, independent cancers occur at higher rates in patients who have survived a primary cancer than in a cancer-naïve population?

PQD4: What are the mechanistic bases for differences in cancer drug metabolism and toxicity at various stages of life?

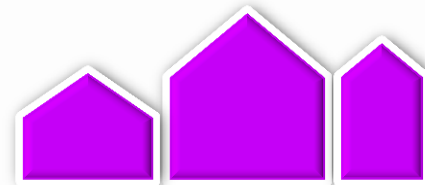
Bringing In New Perspectives

PHYSICAL SCIENCES —
in ONCOLOGY

CENTER for
STRATEGIC
SCIENTIFIC INITIATIVES

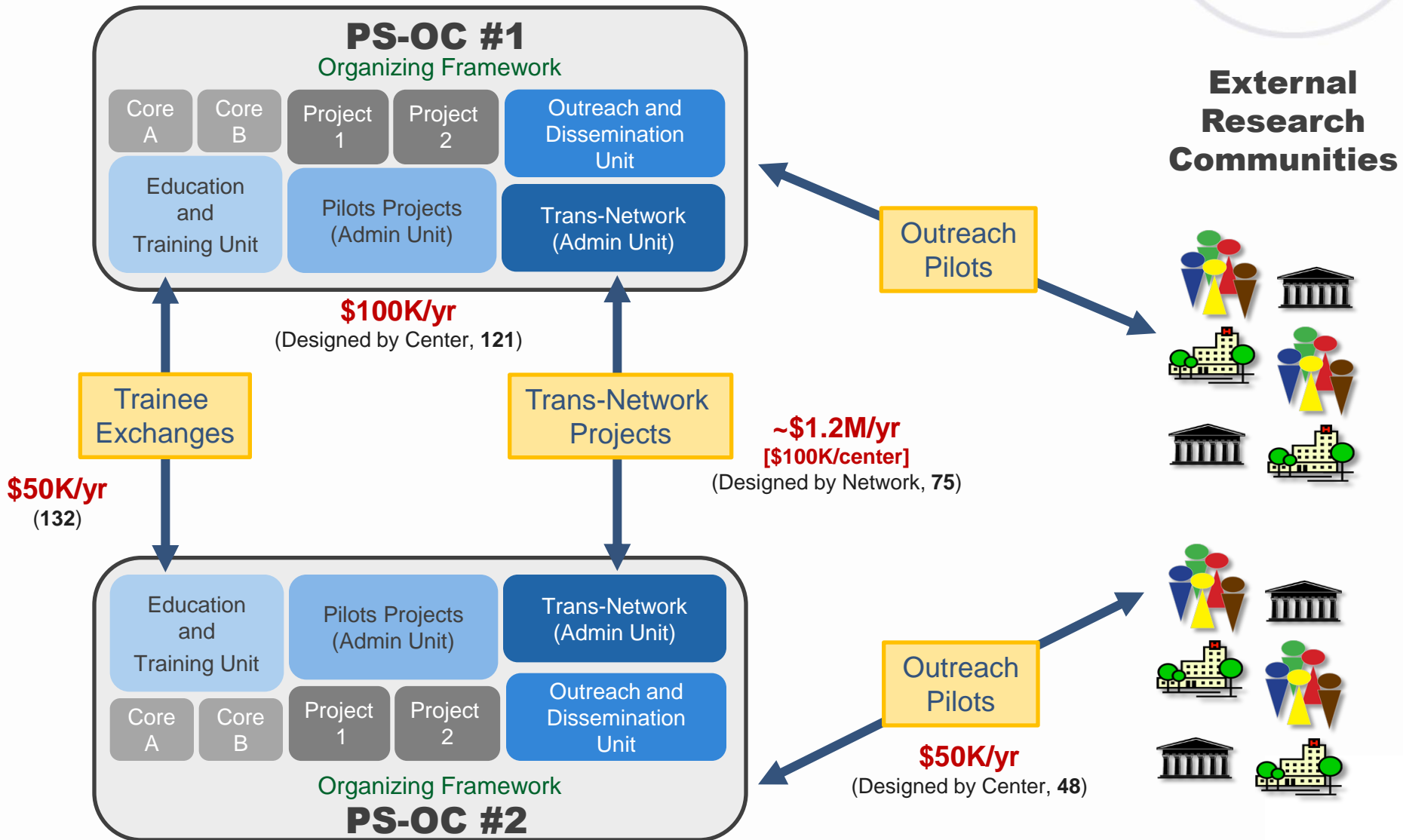


- To generate *new knowledge* and catalyze *new fields of study* in cancer research by utilizing physical sciences/engineering principles to enable a better understanding of cancer and its behavior at all scales.
- Not looking for new tools to do “better” science, but new perspectives and approaches to do *paradigm-shifting* science that will lead to exponential progress against cancer.
- Build *trans-disciplinary teams* and infrastructure to better understand and control cancer through the convergence of physical sciences and cancer biology.



New – “Schools of Thought”

PS-OC Model: PI Driven Interactions Inside/Outside of Network/Center



Then...(2002)



Now...(2014): Moore's Law of Analysts?



200+

Disease working group Matthew Meyerson^{1,2,6}, Stephen B. Baylin²⁹, Ramaswamy Govindan³⁰, Rehan Akbani³¹, Jeoma Azodo³³, David Beer³⁴, Ron Bose³⁵, Lauren A. Byers³⁵, David Carbone³⁶, Li-Wei Chang³⁷, Derek Chiang^{1,13}, Andy Chu¹, Elizabeth Chun¹, Eric Collisson³⁸, Leslie Cope³⁹, Chad J. Creighton⁴⁰, Ludmila Danilova⁴¹, Li Ding⁴², Gad Getz⁴³, Peter S. Hammerman^{1,7}, D. Neil Hayes^{44,45}, Bryan Hernandez⁴⁶, James G. Herman⁴⁷, John Heymach⁴⁸, Cristiane Ida⁴⁹, Marcin Imielinski^{1,6}, Bruce Johnson⁵⁰, Igor Jurisica⁵¹, Jacob Kaufman⁵², Farhad Kosari⁵³, Raju Kucherlapati^{1,12}, David Kwiatkowski⁵⁴, Marc Ladanyi^{1,7,18}, Michael S. Lawrence⁴, Christopher A. Maher⁵⁵, Andy Mungall⁵⁶, Sam Ng⁵⁷, William Paz⁵⁸, Martin Peifer⁵⁹, Robert Perry⁶⁰, Gordon Robertson⁶¹, Valerie Rusch⁶², Chris Sander¹⁶, Nikolaus Schultz¹⁶, Ronlai Shen³¹, Jill Siegfried⁶³, Rileen Sinha¹⁶, Andrey Svachenko⁶⁴, Carrie Soung⁶⁵, Dominik Stoll^{1,50}, Joshua Stuart⁶⁶, Roman K. Thomas^{67,68}, Sandra Tomaszek⁶⁹, Ming-Sound Tsoo⁷⁰, William D. Travis⁷¹, Charles Vaksc⁷², John N. Weinstein^{33,34}, Daniel Weisenberger⁴¹, David Wheeler⁴³, Dennis A. Wagle³³, Matthew D. Wilkerson³³, Christopher Wilks³⁰, Ping Yang⁷³, Jianhua Zhang⁷⁴

Genome characterization centres: BC Cancer Agency Andy Chu¹, Hye-Jung L. Chun⁷, Andrew J. Mungall⁵⁶, Erin Pleasance⁷, A. Gordon Robertson⁶¹, Payal Sipahimalani⁷, Dominik Stoll¹, Mirna Balasundaram⁷, Inanc Birol⁷, Yaron S. N. Butterfield⁷, Eric Chuah⁷, Robin J. N. Coops⁷, Richard Corbett⁷, Noreen Dhalla⁷, Renabir Guin⁷, An He⁷, Carrie Hirst⁷, Martin Hirst⁷, Robert A. Holt⁷, Darlene Lee⁷, Haiyan J. Li⁷, Michael Mayo⁷, Richard A. Moore⁷, Karen Mungall⁷, Ka Ming Nip⁷, Adam Oldren⁷, Jacqueline E. Schein⁷, Jared R. Slobodan⁷, Angela Tam⁷, Nina Thessen⁷, Richard Vorhof⁷, Thomas Zeng⁷, Yongjun Zhao⁷, Steven J. M. Jones⁷, Marco A. Marra⁷; **Broad Institute** Gordon Saksena¹, Andrew D. Cherniack¹, Stephen E. Schumacher¹, Barbara Tabak¹, Scott L. Carter¹, Nam H. Pho¹, Huy Nguyen¹, Robert C. Onofrio¹, Andrew Crenshaw¹, Kristin Ardlie¹, Rameen Beroukhi^{1,2}, Wendy Winkler^{1,5}, Peter S. Hammerman^{1,7}, Gad Getz^{1,2}, Matthew Meyerson^{1,2,6}; **Brigham & Women's Hospital/Harvard Medical School** Alexes Protopopov^{41,10}, Jianhua Zhang⁷⁴, Angela Hadjipapanis^{11,2}, Semin Lee¹, Ruitin Xi¹³, Lixing Yang¹, Xiaojia Ren^{1,12}, Hallel Zhang¹⁹, Sachet Shukla⁹, Peng-Chieh Chen^{1,12}, Psalm Haseley^{1,12}, Eunjung Lee^{12,13}, Lynda Chin^{12,9,10,14}, Peter J. Park^{12,9}, Raju Kucherlapati¹²; **Memorial Sloan-Kettering Cancer Center (COCA pilot phase)** Nicholas D. Socci³⁸, Yupu Liang¹⁶, Nikolaus Schultz¹⁶, Laetitia Borsu¹⁶, Alex E. Lash¹⁶, Agnes Viale¹⁶, Chris Sander¹⁶, Marc Ladanyi^{17,18}; **University of North Carolina at Chapel Hill** J. Todd Auman^{9,20}, Katherine A. Hoadley^{21,22,23}, Matthew D. Wilkerson²⁴, Yan Shi²⁵, Christina Liqior²⁶, Shaowu Meng²⁷, Ling Li²⁸, Yidi J. Turman²⁹, Michong Gang³⁰, Anam Akbar³¹, Nicholas D. Socci³², Elizabeth Buds³³, Jesse Walsh³³, Corbin D. Jones³³, Piotr A. Mieczkowski³³, Darshan Singh³³, Juriyuan Wu³³, Anisha Gulabani³³, Peter Dolins³³, Tom Bodenheimer³³, Alan P. Hovley³³, Janae V. Simons³³, Matthew G. Soloway³³, Lisle E. Mose³³, Stuart R. Jefferys³³, Saisanand Balu³³, Brian D. O'Connor³³, Jan F. Prins³³, Jinze Liu³³, Derek Y. Chang³³; **D. Neil Hayes**^{44,45}, Charles M. Perou^{1,2,22,23}; **University of Southern California/Johns Hopkins Leslie Cope**³⁹, Ludmila Danilova⁴¹, Daniel J. Weisenberger⁴¹, Dennis T. Maglinte⁴⁰, Fei Pan⁴⁰, David J. Van Den Berg⁴⁰, Timothy Triche Jr⁴⁰, James G. Herman⁴⁷, Stephen B. Baylin²⁹, Peter W. Laird³⁹

Genome data analysis centres: Broad Institute Gad Getz^{1,2}, Michael Noble³, Doug Voet¹, Gordon Saksena¹, Nils Gehlenborg^{1,3}, Daniel DiCara¹, Jintua Zhang^{1,10}, Hallel Zhang¹⁹, Chang-Jun Wu^{1,10}, Spring Yingchun Liu¹, Michael S. Lawrence⁴, Lihua Zou¹, Andrey Svachenko⁶⁴, Pei Lin¹, Peter Stigson¹, Rui Jing¹, Juck Cho¹, Marc-Danie Nazaire¹, Jim Robinson¹, Helga Thorvaldsdottir¹, Jill Mesirov¹, Peter J. Park^{12,13,15}, Lynda Chin^{12,9,10,14}; **Memorial Sloan-Kettering Cancer Center** Nikolaus Schultz¹⁶, Rileen Sinha¹⁶, Giovanni Ciriello¹⁶, Ethan Cerami¹⁶, Benjamin Gross¹⁶, Anders Jacobsen¹⁶, Jianyong Gao¹⁶, B. Arman Akbar¹⁶, Nils Weinhold¹⁶, Ricardo Ramirez¹⁶, Barry S. Taylor¹⁶, Yevgeniy Antipin¹⁶, Boris Reva¹⁶, Ronghai Shen¹⁶, Oxanqing Mo¹⁶, Venkatraman Seshan¹⁶, Paul K. Pak¹⁶, Marc Ladanyi^{17,18}, Chris Sander¹⁶; **The University of Texas MD Anderson Cancer Center** Rehan Akbani³¹, Niansheng Zhang³², Bradley M. Brummett³², Cassian³², Anna Urusu³², Chris Wakefield³², Craig Cason³², Keith A. Baggerly³², John N. Weinstein^{33,34}; **University of California Santa Cruz/Buck Institute** David Haussler^{63,7}, Christopher C. Benz³⁴, Joshua M. Stuart³⁵, Jingchun Zhu³⁶, Christopher Szeto³⁷, Gary K. Scott³⁸, Christina Yu³⁹, Sam Ng⁴⁰, Ted Goldstein⁴¹, Peter Waltman⁴², Aram Sokolov⁴³, Kyle Elliott⁴⁴, Eric A. Collisson⁴⁵, Daniel Zerbinio⁴⁶, Christopher Wilks³⁶, Singer³⁶, Margo Crahan⁴⁶; **University of North Carolina at Chapel Hill** Matthew D. Wilkerson³³, J. Todd Auman^{9,20}, Katherine A. Hoadley^{21,22,23}, Ying Du²⁴, Christopher Cabanski²⁵, Vonn Water²⁶, Darshan Singh²⁷, Junyuan Wu²⁸, Anisha Gulabani²⁹, Tom Bodenheimer³⁰, Alan P. Hovley³¹, Janae V. Simons³², Matthew G. Soloway³³, Lisle E. Mose³³, Stuart R. Jefferys³³, Saisanand Balu³³, D. J. Marron⁴⁰, Yufeng Liu²⁴, Kai Wang²⁷, Jinze Liu²⁸, Jan F. Prins³³, D. Neil Hayes^{44,45}, Charles M. Perou^{1,2,22,23}; **Baylor College of Medicine** Chad J. Creighton⁴⁰, Yiqun Zhang⁴¹

~150

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Genome data analysis centres: Broad Institute Gad Getz^{1,2}, D. Voet³, G. Saksena³⁵, Junhua Zhang⁷⁴, H. Zhang⁴⁹, C. J. Wu⁴⁹, S. Shukla⁴⁹, K. Obyedkic^{35,36}, M. S. Lawrence³⁷, A. Svachenko⁶⁴, R. Jing³⁷, R. W. Park^{35,51}, Y. Liu⁴⁹, J. Park^{51,53}, M. Noble³⁷, L. Chin^{35,50,51}, Johns Hopkins University H. Carter⁴⁹, D. Kim⁴⁹, R. Karichin⁴⁹; **Lawrence Berkeley National Laboratory** P. T. Spellman⁶⁶, E. Purdom⁶³, P. Neuvai⁶³, H. Bengtsson⁶³, S. Durnick⁶³, J. Han⁶³, J. E. Korokai⁶³, L. M. Hesser⁶³, R. Cho⁶³, Z. Hu⁶³, B. Parvin⁶², T. P. Speed^{52,66}, J. W. Gray⁶⁷; **Memorial Sloan-Kettering Cancer Center** N. Schultz¹⁶, E. Cerami¹⁶, B. S. Taylor¹⁶, A. Oldren¹⁶, A. Svachenko⁶⁴, Y. Antipin¹⁶, R. Shen¹⁶, P. Markovits¹⁶, R. Sheridan¹⁶, C. Ciriello¹⁶, W. K. Chang^{16,77}, J. A. Bertram¹⁶, L. Borsu¹⁶, D. A. Levine³, M. Ladanyi⁶⁸, C. Sander⁶⁹; **University of California Santa Cruz/Buck Institute** D. Haussler⁶³, C. C. Benz³⁴, J. M. Stuart³⁵, S. C. Benz³⁴, J. Z. Sanborn³⁵, C. J. Vaske³⁶, J. Zhu³⁶, C. Szeto³⁷, G. K. Scott³⁸, C. Yu³⁹; **University of North Carolina at Chapel Hill** K. A. Hoadley^{17,23}, Y. Du³, S. Balu³, D. N. Hayes^{3,4}, C. M. Perou^{1,2,23}; **D. M. Wilkerson**³³; **The University of Texas MD Anderson Cancer Center** J. Zhang³⁸, R. Akbani³⁸, K. A. Baggerly³⁸, W. K. Ying³⁸, G. B. Mills^{20,21}, J. N. Weinstein³⁸

Integrated genomic analyses
of ovarian carcinoma

The Cancer Genome Atlas Network*

Comprehensive genomic characterization
of squamous cell lung cancers

The Cancer Genome Atlas Network*

Comprehensive genomic characterization
defines human glioblastoma genes and
core pathways

The Cancer Genome Atlas Research Network*

2008

2010

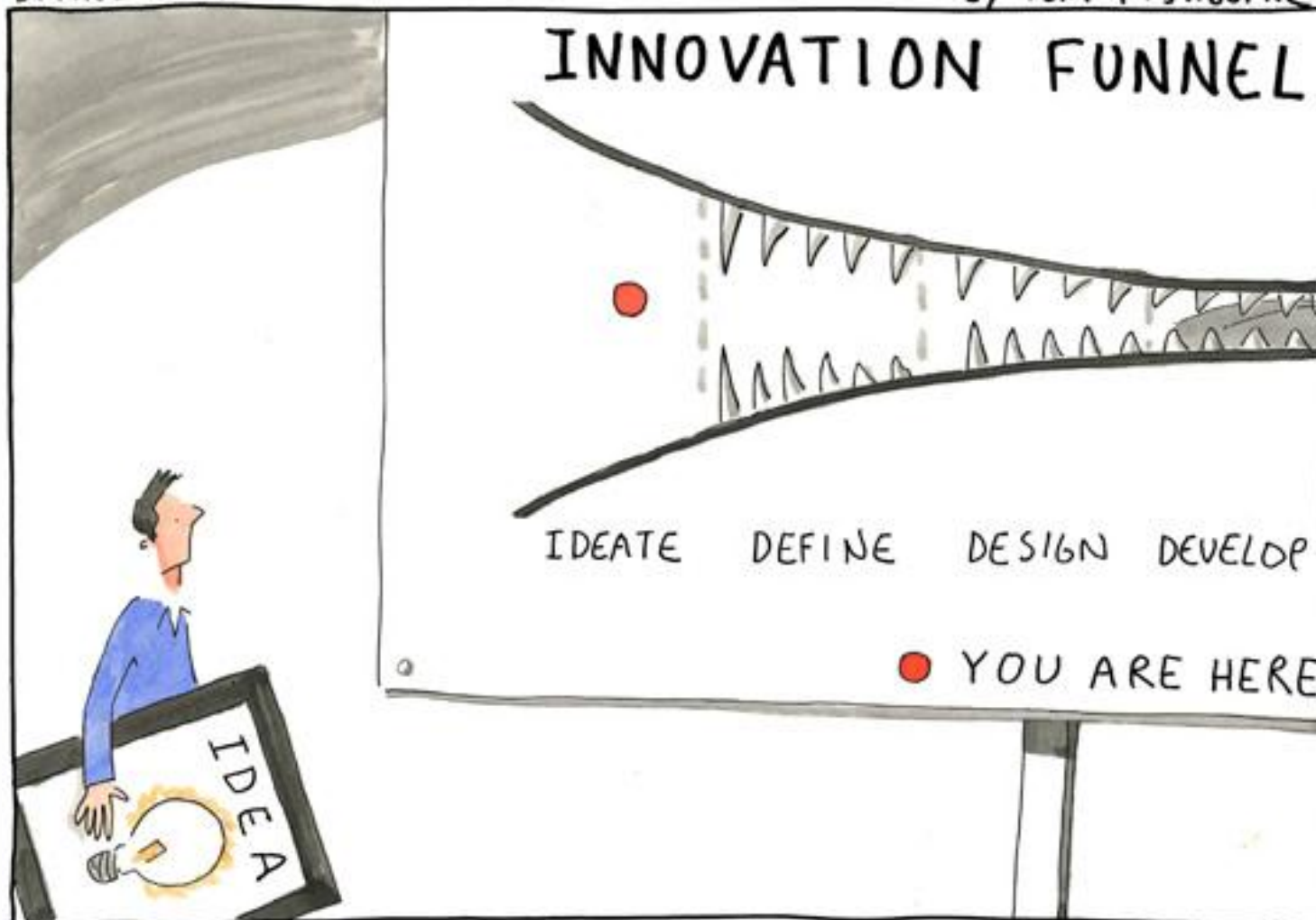
2012

2014



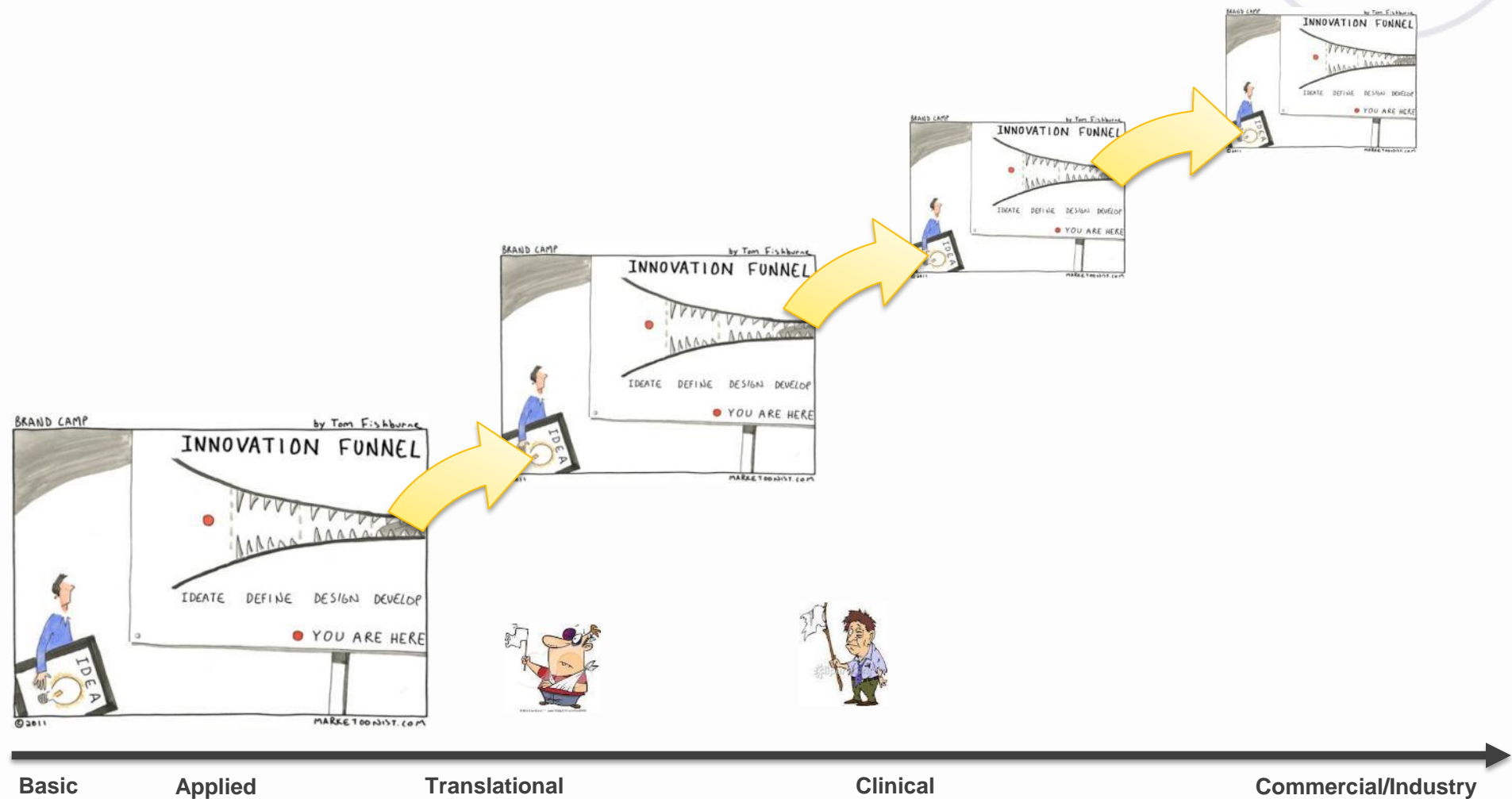
BRAND CAMP

by Tom Fishburne

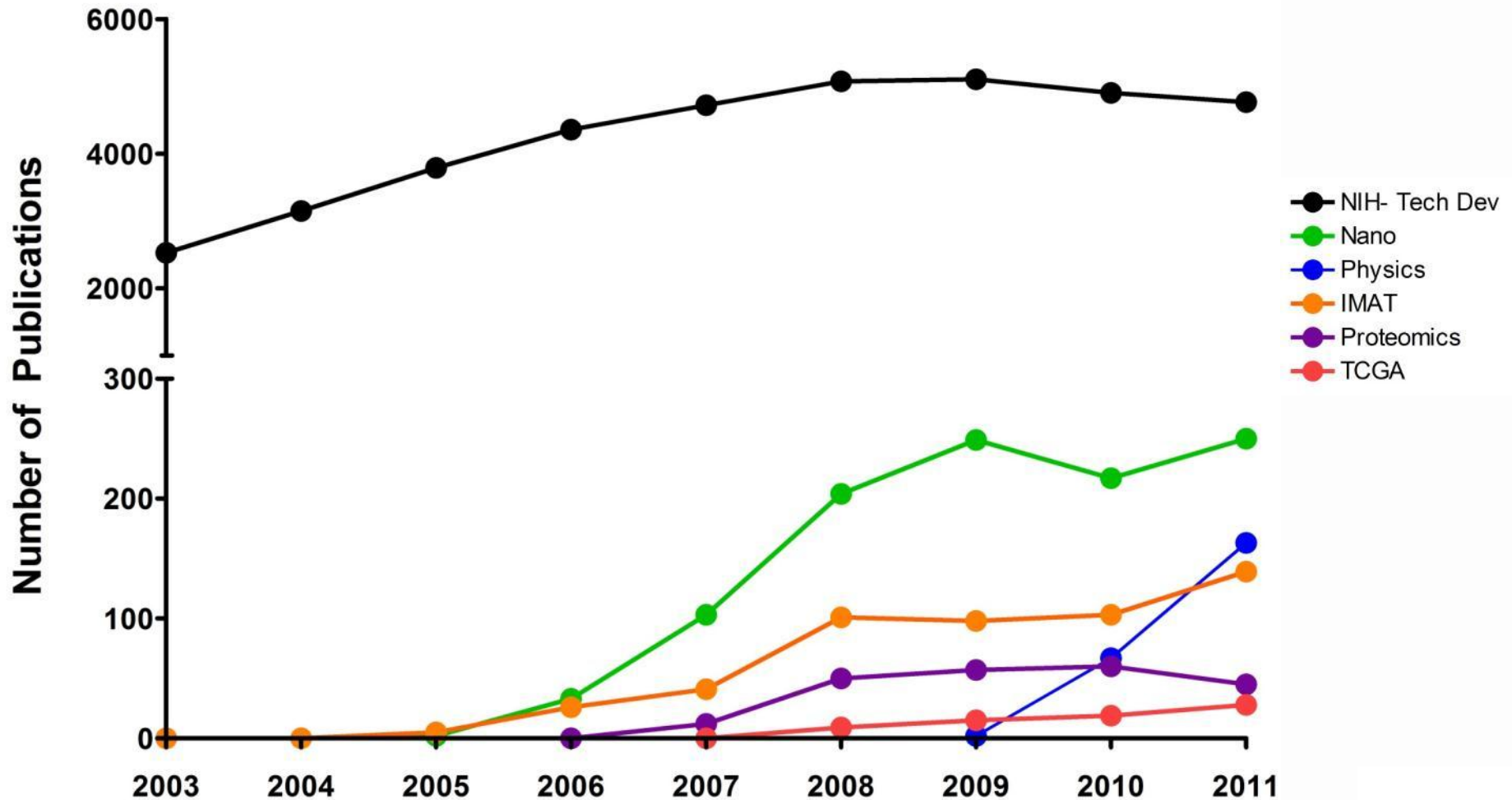


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Need to Look Beyond Publications



CSSI Programs and Evaluations (2004-2014)

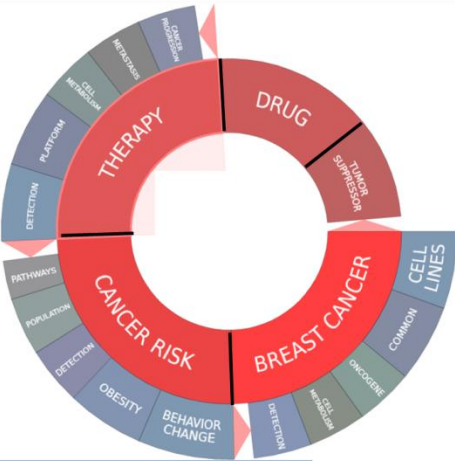


*Red Denotes Eval and/or Changes to Programs

Join the Team!

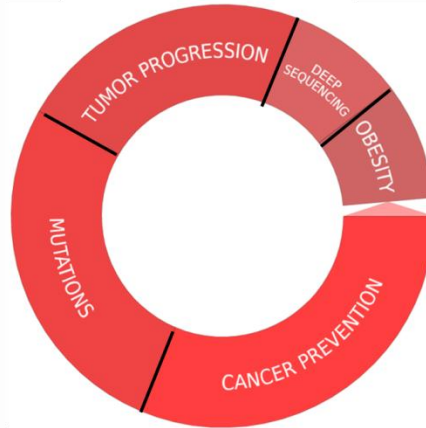
Upcoming Funding Opportunities

R01s



Data from projectreporter.nih.gov

R21s



Provocative Questions (\$30M)

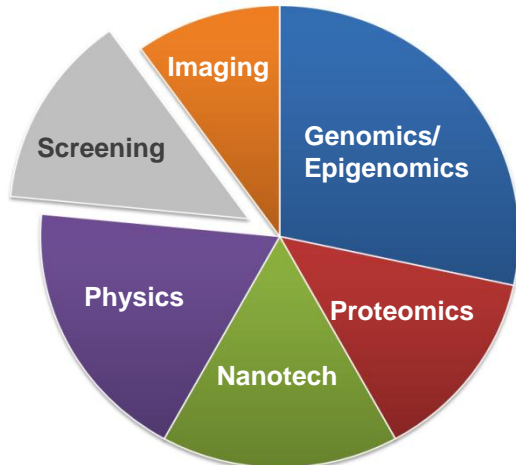


Due Date 06/20/14

PQ Program Director

emily.greenspan@nih.gov

Innovative Molecular Analysis Technologies (\$10.5M)



Due Dates 05/20 and 9/18/14



IMAT Program Director

anthony.dickherber@nih.gov

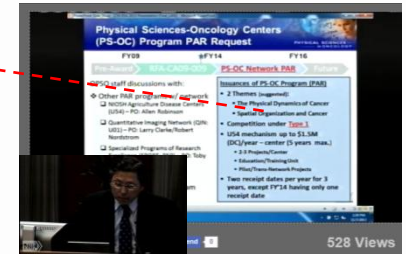


Join the Team!

Upcoming Network Funding Opps



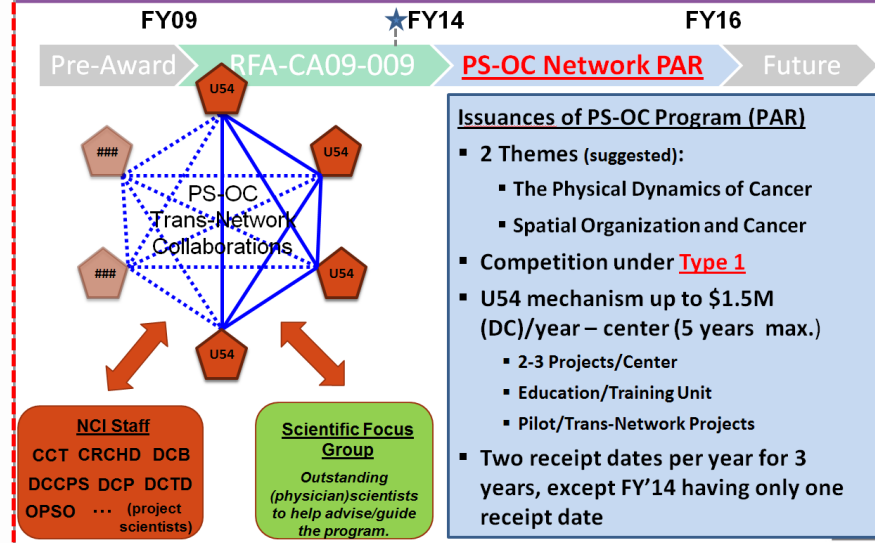
Discussion from NCI Board of Scientific Advisors (Nov 2013)



<http://videocast.nih.gov/launch.asp?18159>

*<http://grants.nih.gov/grants/guide/notice-files/NOT-CA-14-028.html>

Proposed PS-OC PAR Program FY'14-FY'16: Organization and Process



PS-OC Program*



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NCI Alliance for Nano Program (Approved 3/2014)

Cancer Research



Future Opportunities in Cancer Nanotechnology - NCI Strategic Meeting Report

Piotr Grodzinski and Dorothy Farrell

Cancer Res Published OnlineFirst January 10, 2014.



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Summary of Responses to RFI on Directions and Needs for Cancer Nanotechnology Research and Development

The National Cancer Institute Office of Cancer Nanotechnology Research published a summary of its request for information on the Directions and Needs for Cancer Nanotechnology Research and Development. The purpose of the RFI was to gain feedback, comments and ideas from the extramural community, as well as NCI Alliance leaders, investigators, trainees and related spin-offs, on the status and future of the field and the role NCI funding has played and should continue to play in the future.

Relevant CSSI Funding Opportunities

- **Research Answers to NCIs Provocative Questions- Group A-E (R01)**
 - **Due Date: 06/20/2014** RFA-CA-13-016, 018, 020, 022,024 (\$2-3M each RFA, \$10-\$15M total)
- **Research Answers to NCIs Provocative Questions- Group A-E (R21)**
 - **Due Date: 06/20/2014** RFA-CA-13-017, 019, 021, 023, 025 (\$0.5-1M each RFA, \$2.5M - \$5M total)
- **Early-Stage Innovative Molecular Analysis Technology Development (R21)**
 - **Due Date: 05/20/2014 and 09/18/2014** RFA-CA-14-003 (\$5M)
- **Validation and Advanced Development of Emerging Molecular Analysis Technologies (R33)**
 - **Due Date: 05/20/2014 and 09/18/2014** RFA-CA-14-004 (\$4M)
- **Early-Stage Development of Innovative Technologies for Biospecimen Science (R21)**
 - **Due Date: 05/20/2014 and 09/18/2014** RFA-CA-14-005 (\$0.8M)
- **Validation and Advanced Development of Emerging Technologies for Biospecimen Science (R33)**
 - **Due Date: 05/20/2014 and 09/18/2014** RFA-CA-14-006 (\$0.7M)



Relevant NCI Funding Opportunities

- **Innovative Molecular Analysis Technology Development for Cancer Research and Clinical Care (R43/R44)**
 - Due Date: 5/28/2014 and 11/4/2014 PAR-13-327

- **Early-Stage Development of Informatics Technology (U01)**
 - Due Date: 6/18/2014 and 11/18/2014 PAR-12-288

- **Advanced Development of Informatics Technology (U24)**
 - Due Date: 6/18/2014 and 11/18/2014 PAR-13-294

- **Imaging and Biomarkers for Early Cancer Detection (R01)**
 - Due Date: 7/10/2014 and 12/11/2014 PAR-13-189

- **Image-guided Drug Delivery in Cancer (R01)**
 - Due Date: 6/19/2014 and 11/19/14 PAR-13-185

- **Biomarkers for Early Detection of Hematopoietic Malignancies (R21/R01)**
 - Due Date: 6/16/2014 (R21) & 7/5/2014 (R01) [Standard] PA-12-220 (R21) & PA-12-221 (R01)



Acknowledgements/Thanks to the “Secret Ingredients”

Clinical Sciences



Life Sciences



Physical Sciences



Learn More About Us...



<http://cssi.cancer.gov>

The screenshot shows the homepage of the Center for Strategic Scientific Initiatives (CSSI). At the top, there is a red banner with the National Cancer Institute logo and the text "National Cancer Institute" and "U.S. National Institutes of Health | www.cancer.gov". Below this is the CSSI logo and a navigation menu with links for "HOME", "ABOUT CSSI", "CSSI OFFICES", and "CONTACT CSSI". The main content area features a large image of a DNA double helix and the text: "ENABLING PROGRESS IN CANCER RESEARCH THROUGH ADVANCED TECHNOLOGIES, TRANS-DISCIPLINARY PROGRAMS".

Jerry S.H. Lee, PhD
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This screenshot shows the "Timeline" feature of the CSSI website. It includes a "Timeline:" heading, a selection of offices (OD CSSI, OBRR, TUGA, OCG, OCCPR, OCNR, OPSO), and a "Zoom Level:" section with options for 1 Year, 3 Years, and All Years. The main area displays a timeline from 2000 to 2012 with various circular icons representing events.

This screenshot shows the "RESOURCES" page of the CSSI website. It features a "Current Resources" section with "Funding Opportunities" and "Notices". A specific funding opportunity is highlighted: "CSSI Specific Funding Opportunities: Nanoscience and Nanotechnology in Biology and Medicine (R01) (PA-14-148)". It includes application receipt dates and an expiration date of May 8, 2014. There is also a section for "Relevant NCI Funding Opportunities" with a link to "National Cancer Institute Program Project Applications (Po1)".

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Hope to meet you at the conference. Thomas Peterson
(Chief of Bioengineering Sciences and Technologies)